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1. please read Imtiyaz Murtaza as third author in addition to others 2.Author, M Dhuha is from the **Department of Biotechnology (University of Kashmir) instead of Phychology as mentioned.**

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Prof.GM Malik
Editor-in-Chief

In my previous online editorial I welcomed Dr. Bakshi Jehangir as the driving force behind our new venture - the internet edition of JK Practitioner - with the hope that it would be as warmly recieved as the print version and increase the sphere of influence of our journal. Over the past year this promise has been fulfilled beyond expectations and our website at **www.jkpractitioner.org** is recieving numerous hits daily. An active online presence on the internet has given the international recognition of JK- Practitioner a boost and the Journal is constantly being indexed by prestigious industry-leading sources. A simple internet search for the term "JK- Practitioner" will return links from the likes of :

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Wishing you a happy new year and thanking you for support and suggestions.

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BIOMECHANICS OF SPINAL DEFORMITY.

Suhail Afzal(.MS); Mohd.Ramzan Mir (MS), Munir Farooq (MS); Ghulam Rasul MIr M.Ch. Orth. (L'Pool) FRCS (Edin) FRCS (Orth)

The correction of spinal deformity may be achieved by a variety of methods, each of which has advantages and disadvantages. The goals of spinal deformity surgery include reasonable correction of the curvature, prevention of further deformation, improvement of sagittal and coronal balance, optimization of cosmetic issues, and restoration/ preservation of function. The failure to consider all these factors appropriately may result in a suboptimal outcome. Understanding fundamental biomechanical principles involved in the formation, progression, and treatment of spinal deformities is essential in the clinical decision-making process.

Pathological spinal deformation, either in an acute or chronic form, is usually a result of at least one unstable motion segment. For the deformity to progress, pathological stressors must be applied to an already deformed spine may also cause further deformity. The spine surgeon is faced with significant challenges in formulating treatment strategies for both spinal deformities and deformity progression. Objectives including curvature correction, prevention of further deformity, restoration of sagittal and coronal balance, cosmetic optimization, improvement and preservation of neurological function must be simultaneously considered during treatment planning to optimize successful outcome ^{2} . Spinal deformities are complex entities, often composed of more than one deformation type with more than one attendant problem. A complex solution can be achieved by combining component strategies for each aspect of the complex problem. Awareness of the complexities of deformation development and progression is critical to the design of an appropriate management scheme. The surgeon must try to understand the forces at play in creating the deformity, which is necessary because during the correction the forces must be countered or reversed, thereby neutralizing the pathological forces. Complete deformity correction is often the goal, but it is not necessarily required to alleviate symptoms and prevent further deformity or neurological deficit. The goal of surgery, hence should be the attainment and maintenance of a nonpathological relationship between the neural elements and their supporting and surrounding osseous and soft tissue structures.

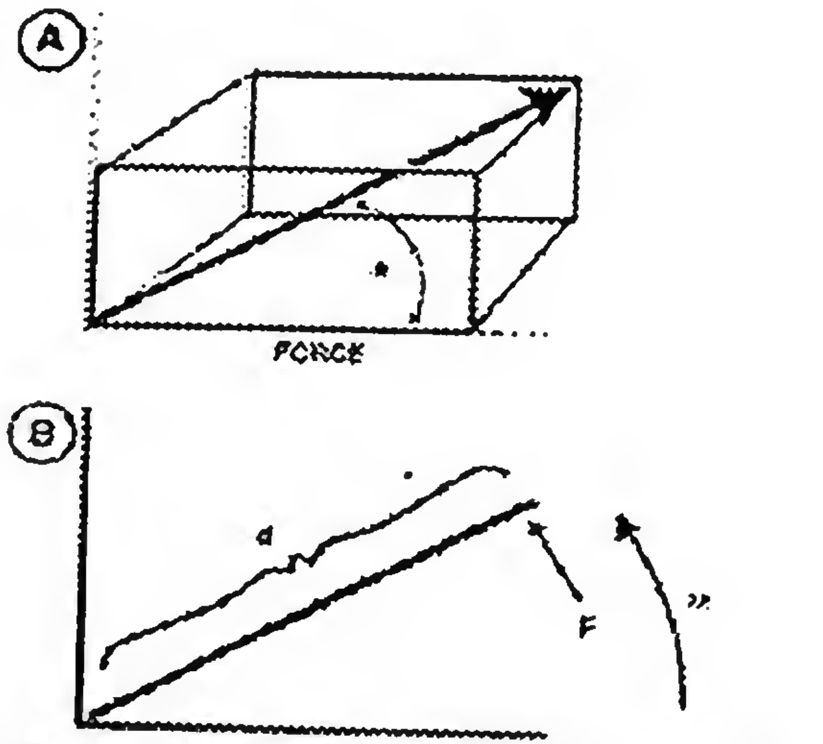

Fig. 1 A: A force vector in three-dimensional space. B: If a force (F) is applied at a distance (d) from a fulcrum (IAR), a bending moment (M) is created.

SPINAL DEFORMITIES.

Physical Principles and Kinematics.

Forces applied to the spine can be broken down into component vectors. A vector is defined as a force oriented in a fixed and well defined direction in three dimensional space. A force vector may act on a lever(moment arm), creating a bending moment. The bending moment applied to a point space causes rotation, or tendency to rotate, around an axis. The axis is termed as IAR. The IAR acts as a pivot point or fulcrum around which flexion or extension occur. The moment arm is a lever that extends from IAR to the position of application of force to the spine(fig.1).

The bending moment (M) is defined as the product of the force(F) applied to the lever arm and length of the lever arm(D) in the following formula: $M= F \times D$. The bending moment is effectively the torque applied by a circular force. The magnitude of a circular force is the

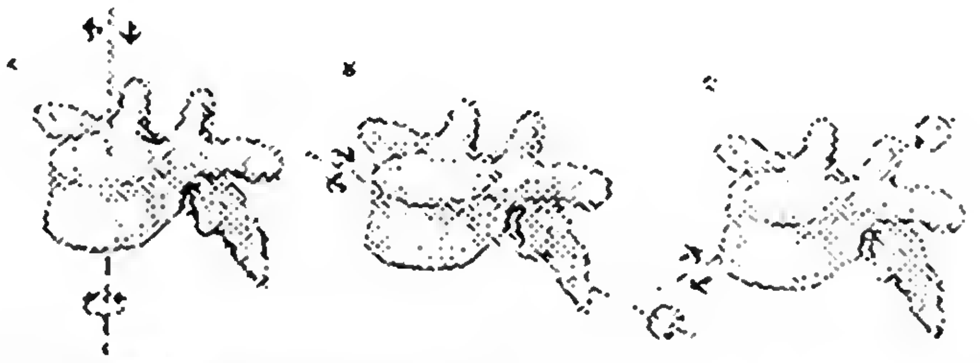

Fig. 2 The six fundamental segmental movements or types of deformation. [illegible]

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torque. Around each of the three axes of the Cartesian coordinate system, translation or rotation can occur. Therefore six fundamental segmental movements of the spine along or around the IAR can occur: 1) rotation or translation around the long axis; 2) rotation or translation around the coronal axis; 3) rotation or translation around the sagittal axis of the spine; 4) translation along the coronal axis; 5)translation along the long axis of spine; 6) translation along the sagittal axis of the spine (Fig.2).Each movement may result in deformation in one of two directions involving one or many spinal segments as a result of acute or chronically applied loads.

Rotational Deformation:

A bending moment affects a spinal segment by the application of an eccentrically placed load(that is,eccentric to the IAR). Angular deformation of the spinal segment may result along one or both of the axially oriented axes following the application of a bending moment.Such rotation can take the form of kyphosis(flexion rotation deformation). lordosis(extension rotation deformation). scoliosis(lateral bending rotation deformation), or a combination of these. Rotational deformations are manifestations of an asymmetrical load or a rotatory load(torque) applied to a spinal segment. Rotational deformations around an axially oriented axis (coronal or sagital) can occur at the level of the VB or intervertebral disc space [5,10,15,32] .Segmental spinal rotatory deformation can occur around the long axis of the spine (Fig. 3).The application of a rotatory or torsional load to the spine can cause the spinal segments above the unstable segment to rotate in a direction in opposition to that below the unstable segment.

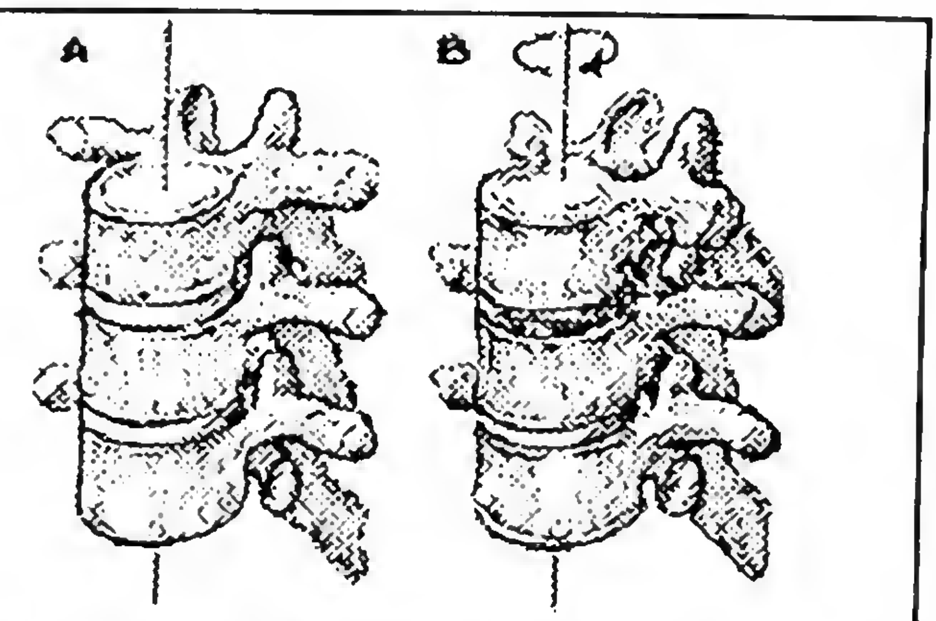

Fig. 3 A twisting of the spine around its long axis (A) can result in a rotatory deformation around the axis (B). *Curved arrow* depicts applied bending moment.

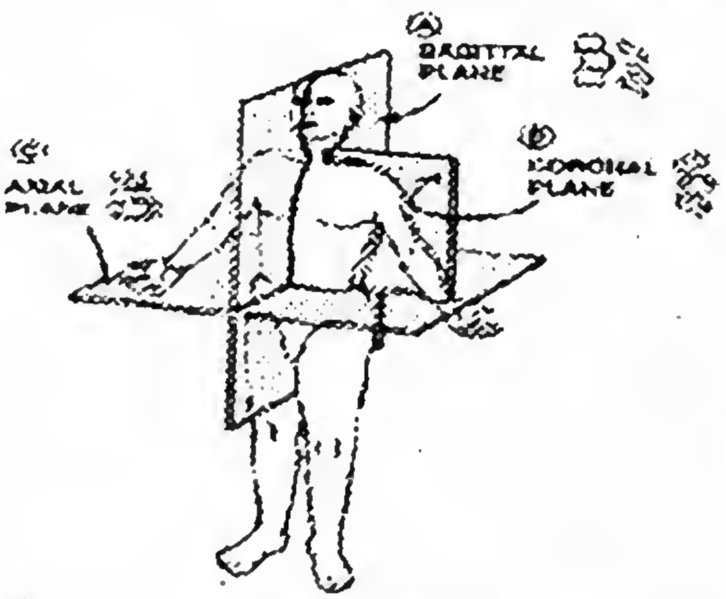

Fig. 4. Sagittal (A), coronal (B) and axial plane (C) delineate the three fundamental deformations that contribute to all spinal deformities, either individually or in combination.

Translational Deformation.

Shearing, compression, or distraction of the spinal segments may result in translational deformation, which occurs along an axis defined by the direction of the deformation-creating force vector [5,15,32] . Translational deformation may occur in any plane. Burst fractures are caused by oppositional translational forces of the upper and lower endplates of a VB. Axially oriented translational deformities occur secondary to two parallel but noncoincident opposed force vectors resulting in fracture dislocation or spondylolisthesis. Distraction deformation is uncommon and usually accompanies a significant flexion component in the acute form. Distraction forces may be applied using spinal traction or by excessive implant-induced distraction. Most spinal deformities, however, are a result of more than one type of deformation.

Fig. 5. [illegible]

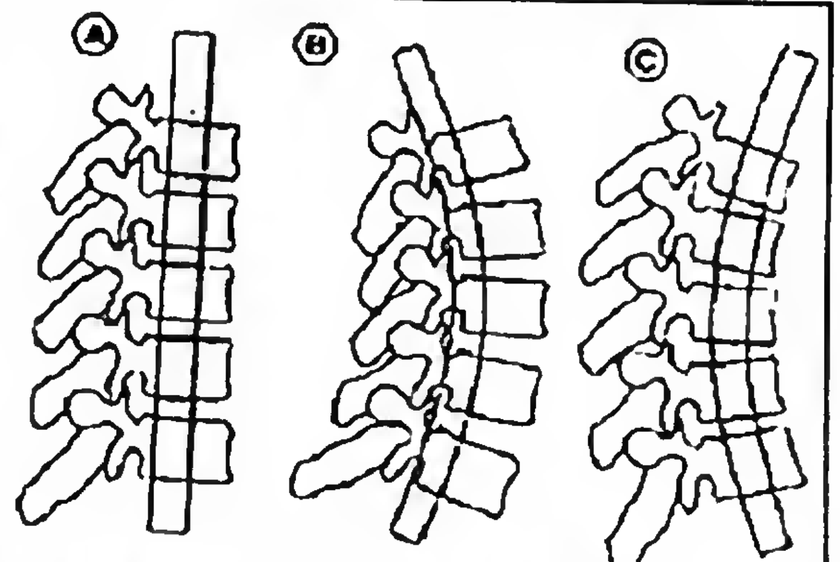

Fig. 6. The load-bearing axis (neutral axis: *shaded region*) (A) is generally considered to be located in the region of the middle column of Denis. In extension, however, the load-bearing axis is shifted dorsally in the cervical spine (B). In flexion it is shifted ventrally (C), and in lateral bending it is shifted laterally toward the concavity of the curve.

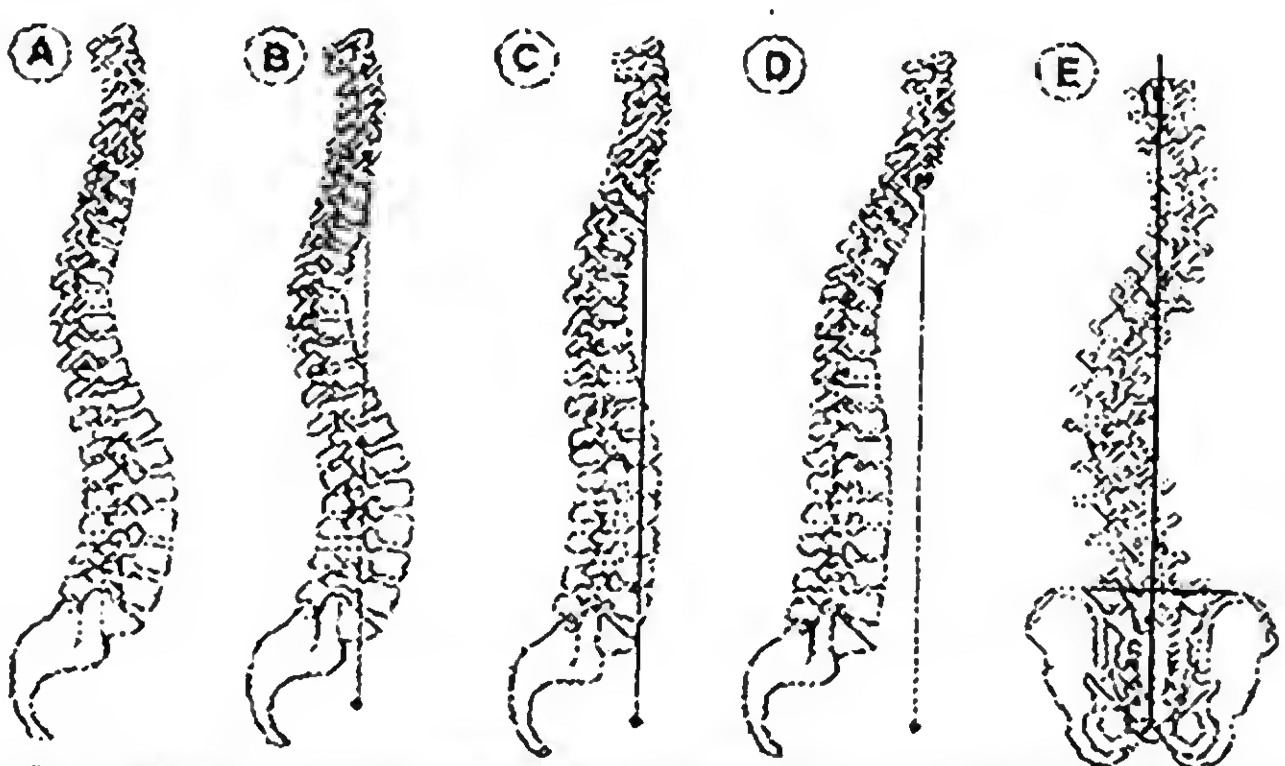

Fig. 7. Sagittal balance. A: A spine in sagittal balance, with a generous but not excessive cervical lordosis, thoracic kyphosis, and lumbar lordosis. B: A plumb line that is dropped from the mid-C-7 VB (SVA) in the standing position falls in the region of the lumbosacral pivot point (normal L5-S1 disc interspace). If the normal spinal contour is disturbed by a focal deformity, balance may be achieved by compensatory mechanisms. C: Note that if loss of lumbar lordosis is present, the SVA falls through the region of the sacral promontory. D: Significant imbalance, however, may be developed, resulting in the SVA falling at a significant distance ventral to the sacral promontory. The CSL is used to assess balance in the coronal plane. E: The CSL is a line that is perpendicular to a line passing through both iliac crests, extending rostrally, in line with spinal spinous processes. The vertebrae bisected by this line are termed stable vertebrae (Modified [illegible])

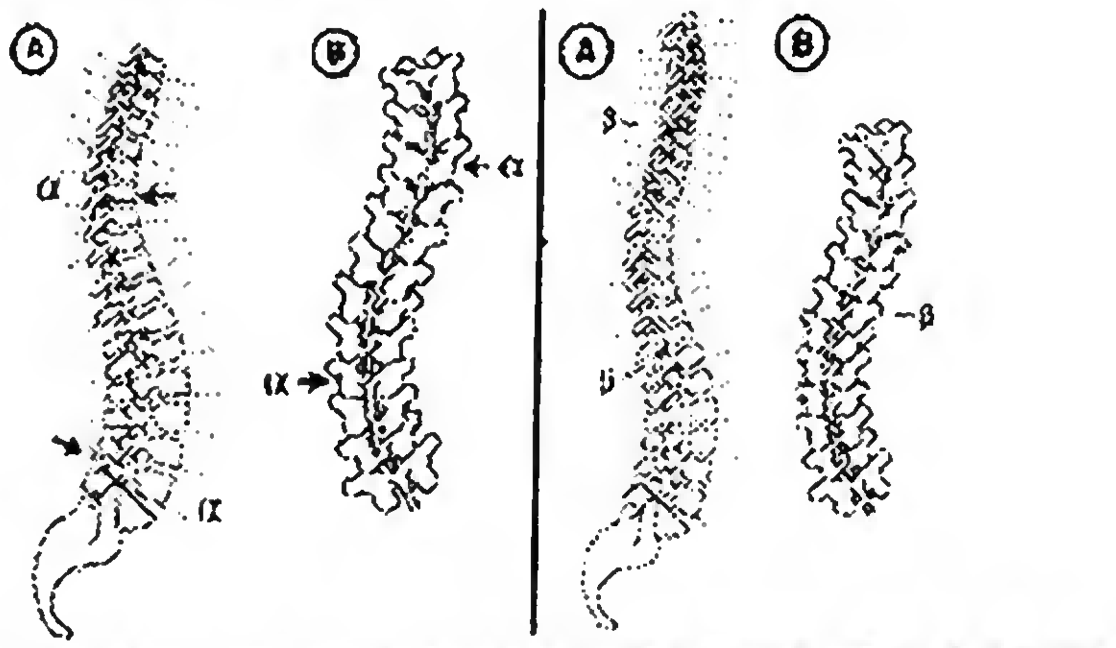

Fig. 8 *Upper:* An apical vertebra occurs at the horizon or apex of a curve, either in the sagittal (A) or coronal plane (B). It is associated with adjacent disc interspaces that have the greatest segmental angulation (α) of all interspaces in the curve, as depicted. *Lower:* The neutral vertebrae are located between curves, be it sagittal (A) or coronal (B). There is little or no angulation at its rostral and caudal disc interspaces (β), as depicted.

Categories of Spinal Deformity:

Spinal deformities may be divided into three fundamental categories: 1) sagittal plane; 2) coronal plane; and 3) axial plane. Many deformities are composed of a combination of sagittal-, coronal-, and axial -plane components (Fig.4). Degenerative lumbar scoliosis is a common deformity resulting in both a rotational and a kyphotic component.

Prevention of Deformity Progression.

Excessive forces affecting the spine and/ or nonpathological stressors affecting an already deformed spine are required to create a deformation or for it to propagate. A working understanding of the neutral axis, Cobb angle, and the radius of the curvature is important in the decision making process when managing cases of spinal deformity. Prevention of kyphotic deformity progression requires knowledge of the neutral axis (load bearing axis). Placement of strut grafts well ventral to the neutral axis helps prevent further kyphotic deformity (Fig.5). Likewise, dorsal constructs must be placed well behind the neutral axis to prevent the progression of kyphosis.

Principles of Deformity Correction.

Many factors must be considered when attempting to correct a spinal deformity. The deformities are frequently multisegmental. Thus, strategies must be applied to multiple spinal segments. A deformity that occurs along or around an axis of the Cartesian coordinate system often produces another motion along or around another axis (that is coupling phenomenon). The load bearing axis in both the sagittal and coronal planes must also be considered. The load bearing axis in the healthy cervical and lumbar regions is located in the dorsal region of the VBs, and in the normal thoracic spine, it is located ventrally. The load bearing neutral axis is usually in the region of the middle column (Fig.6). The neutral axis is shifted ventrally with flexion and dorsally in extension. Sagittal balance of the spine must be considered [16,18,21,28]. In the standing position, a plumb line dropped from the mid C-7 VB, should fall in the region of the dorsal L5-S1 interspace. A negative 2-4 cm space behind this region is normal. A loss of balance may occur, with the sagittal vertebral axis falling quite ventral to S1 (Fig.7). [17,18].

The CSL is used to assess balance in the coronal plane and as well as in the assessment of scoliosis [1]. The CSL is one that is perpendicular to a line passing through both

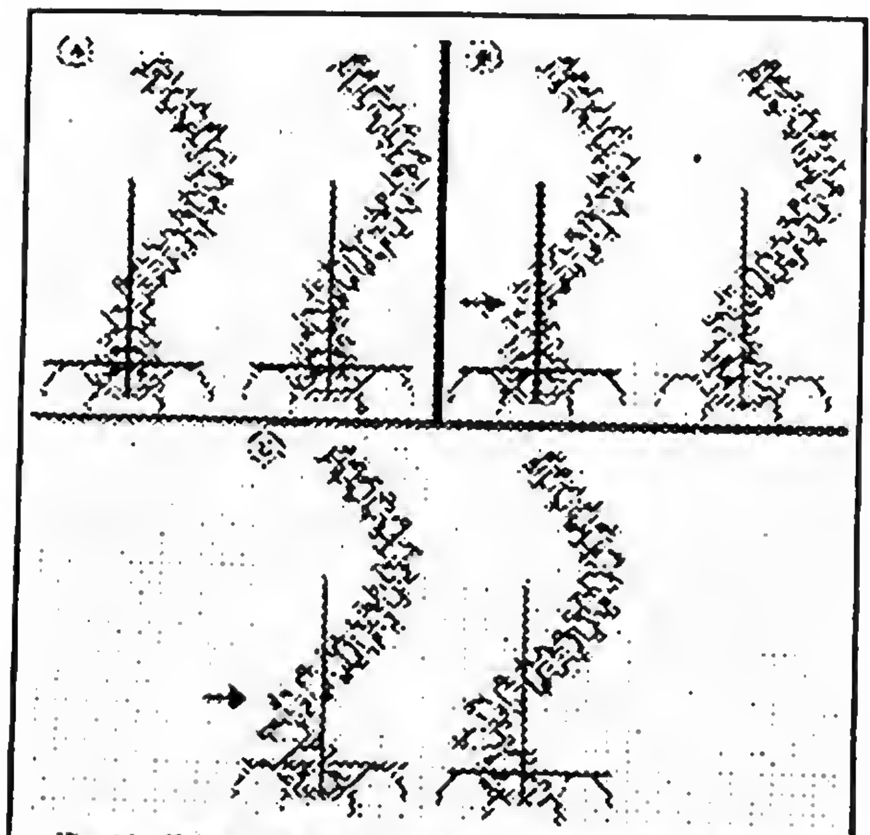

Fig. 11. The definition of complex deformity may be enhanced by the additional use of the scheme proposed by Lenke. This scheme emphasizes the CSL. A: The CSL between pedicles up to the stable vertebra with minimal or no lumbar scoliosis (Lumbar modifier A). B: The CSL touches the apical VB or pedicles (Lumbar modifier B). C: The CSL does not touch apical VB or the VBs immediately above and below the apical disc (Lumbar modifier C) (arrows denote apical vertebrae).

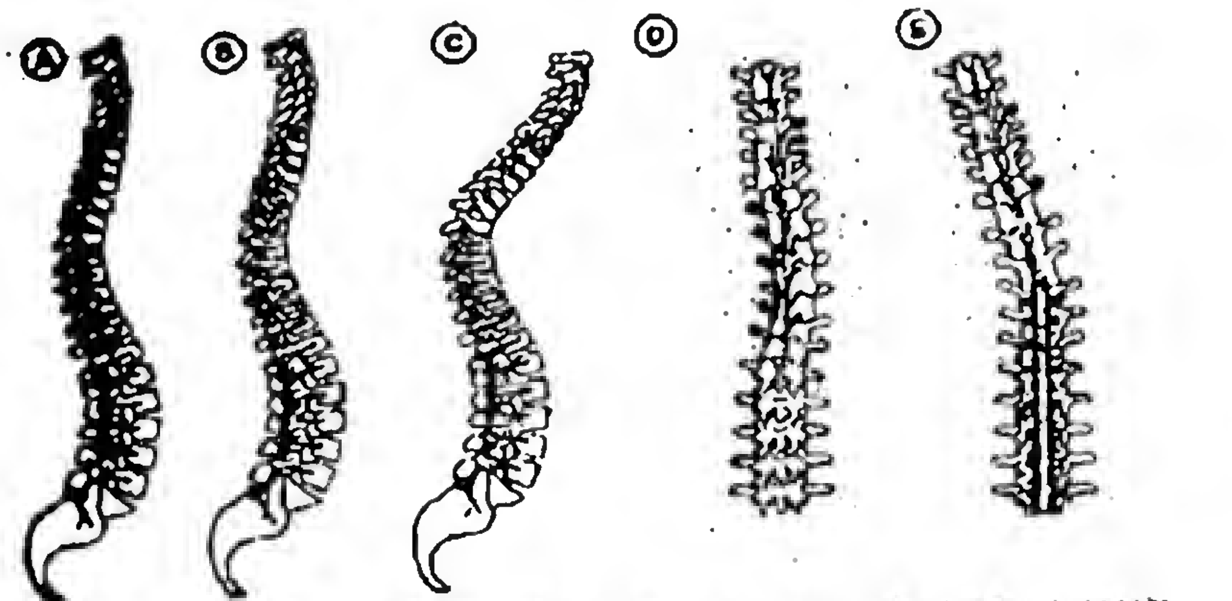

Fig. 9. A: A long implant should usually not terminate at or near an apical vertebra. B: A longer implant may be required. C: Spine deformation at the termini of the implant is to be expected if the implant terminates at the apex of a curve. D: This is also shown for correction of a scoliotic deformity. E: Note postoperative progression of deformity. The implant was placed up to, but not beyond, the apical vertebra.

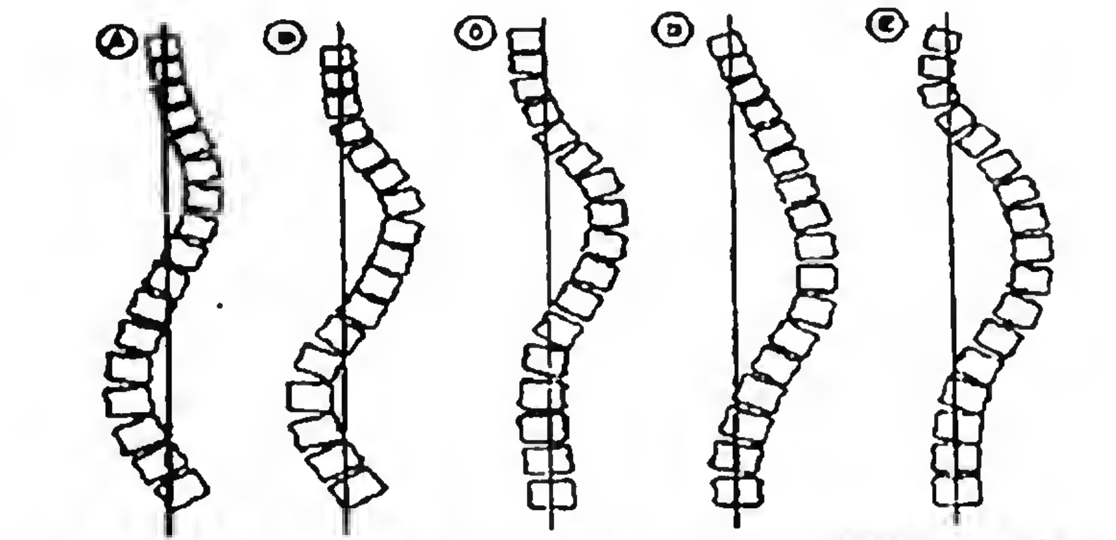

Fig. 10. The King classification scheme for idiopathic scoliosis. A: Type I is a double concave deformity in which the lumbar curve is larger and more rigid than the thoracic curve. B: Type II is a double concave deformity in which the thoracic curve is more rigid. C: Type III is a thoracic curve. D: Type IV is a long thoracic deformity that tilts into the curve. E: Type V is a double thoracic curve that tilts into the concavity

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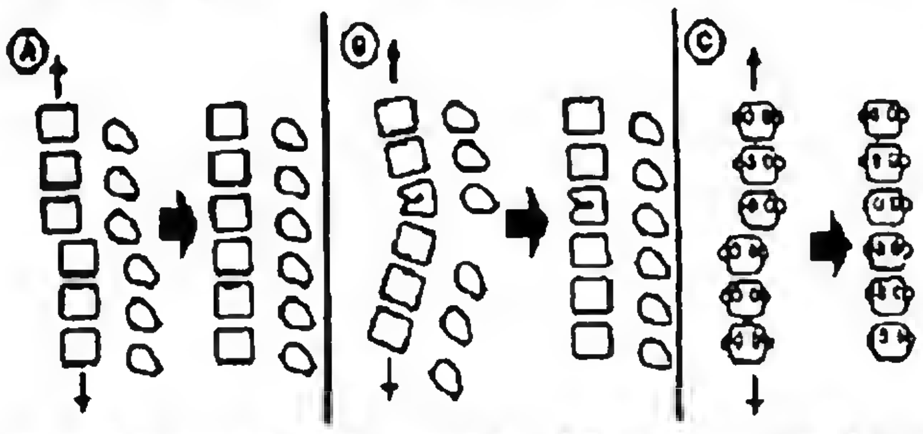

Fig. 12. In "bringing the spine to the implant" forces that are oriented along any axis or plane may be used (for example, the long axis (A), the sagittal plane (B), and the coronal plane (C). *Arrows* depict forces applied by the implant.

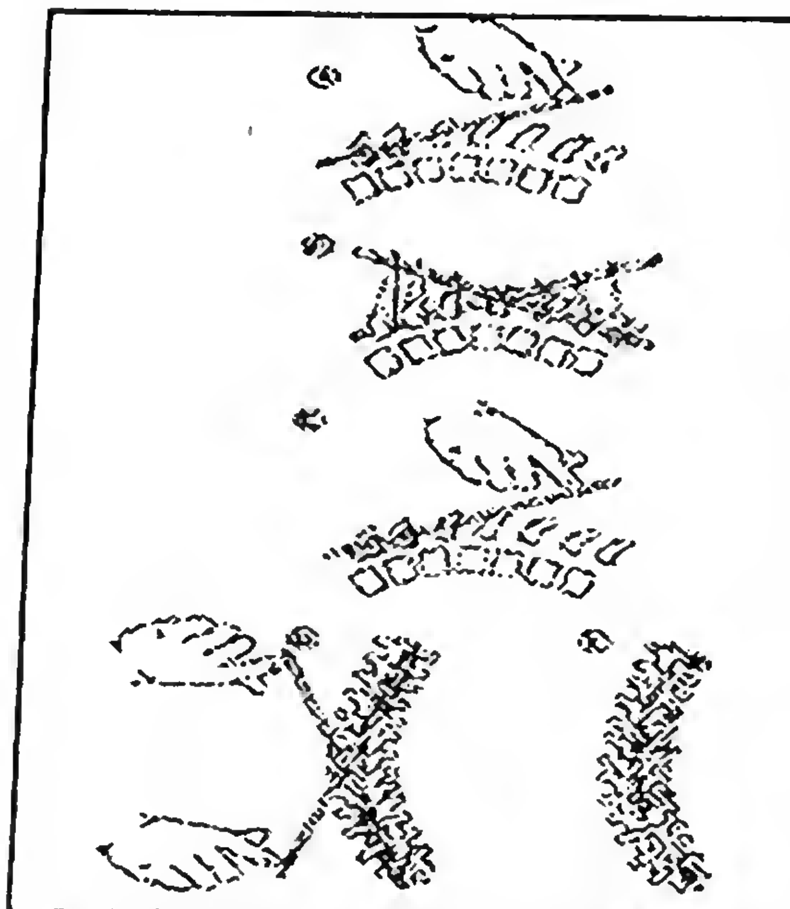

Fig. 14. The crossed-rod technique for correcting thoracic and lumbar kyphotic deformities involving the Harrington distraction rod (A), Luque sublaminar wiring (B), and universal spinal instrumentation (C). The latter technique is facilitated by the use of segmental hook insertion [illegible]. The crossed-rod technique strategy can be used for coronal-plane (scoliotic) deformities as well (D). Two-rod translation [illegible] strategies can similarly be used. In this case, a small rod may be applied to the spine and brought to a longer rod that spans the concave side of the deformity, thus gradually correcting the deformity (E).

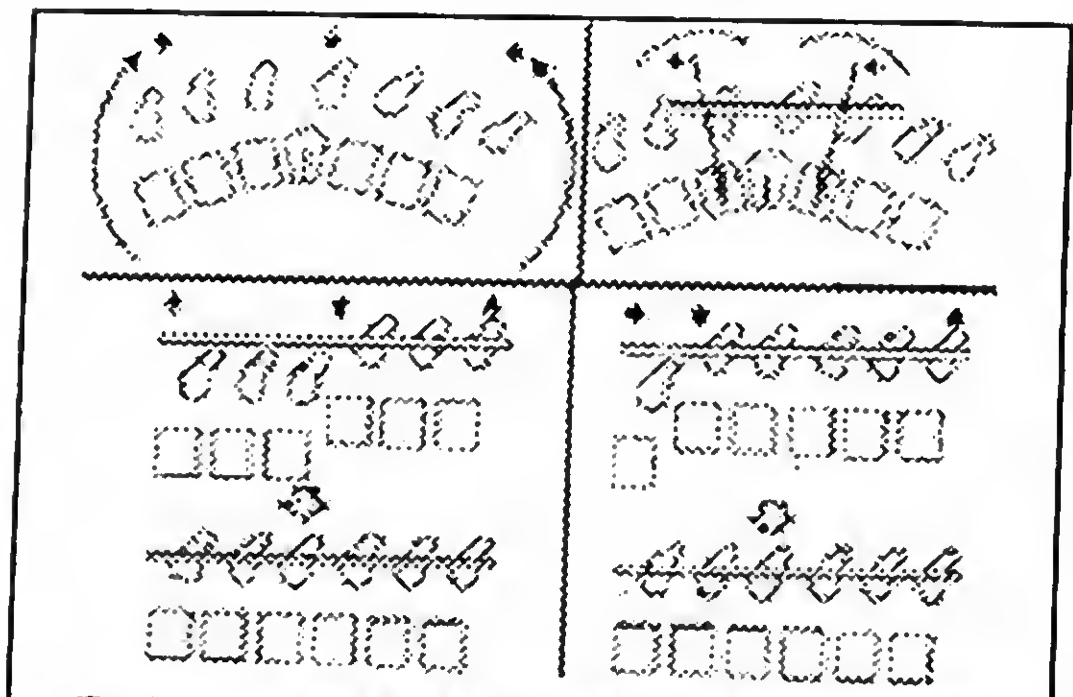

Fig. 13. Bending moments are applied in the sagittal plane by a three-point bending mechanism *(upper left)* and an applied moment arm cantilever beam mechanism *(upper right)*. *Straight arrows* depict forces; *curved arrows* depict bending moments. *Lower Left.* The three-point bending construct brings the spine to the implant. *Lower Right:* The terminal three-point bending constructs simply have one long and one short moment arm. *Straight arrows* depict forces applied.

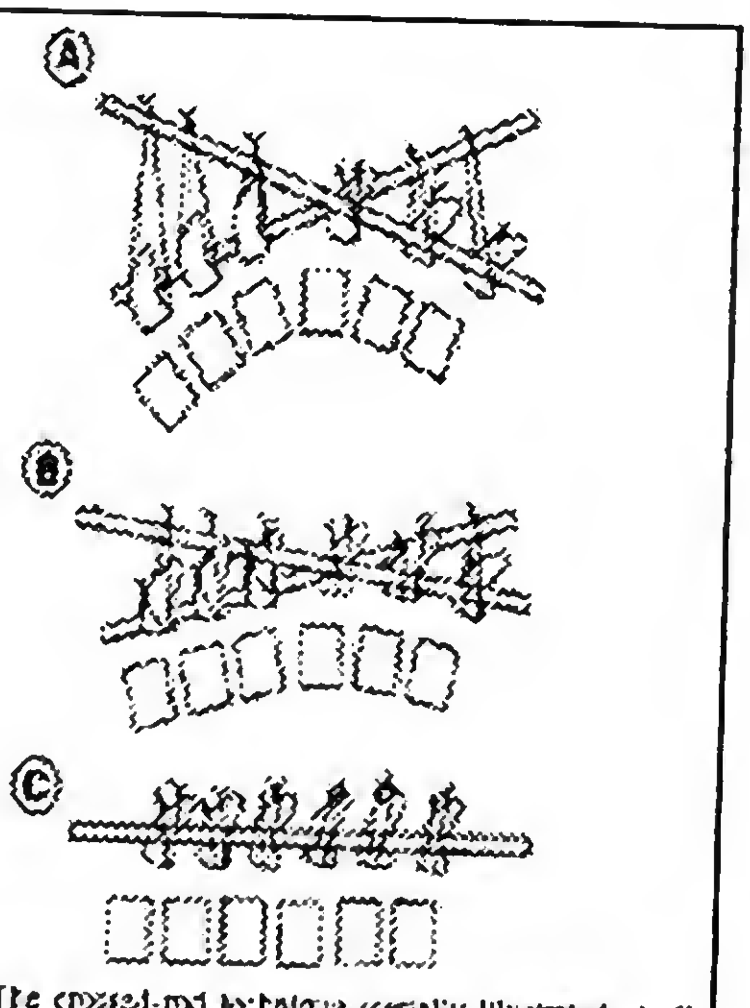

Fig. 15. The crossed-rod technique (serially illustrated, A–C) for achieving gradual reduction of a kyphotic deformity.

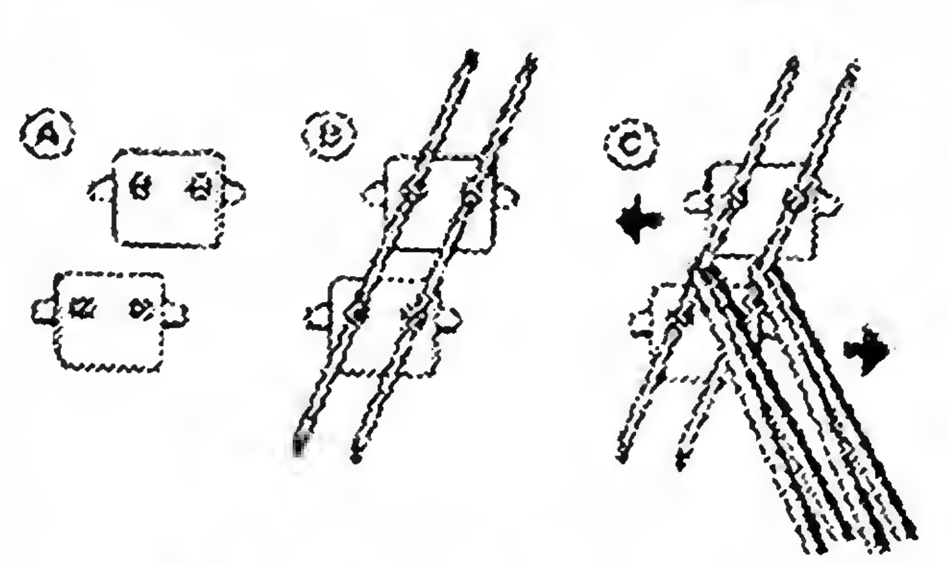

Fig. 16. Short-segment parallelogram reduction of a lateral translational deformity. A: Pedicle screws are placed. B: The pedicle screws are connected by rods. C: The rods are connected (friction-glide tightness) and a torque applied to both rods simultaneously by rod grippers. Reduction is achieved and then maintained using rigid cross-fixation. Distraction, followed by interbody bone graft placement and compression, is used to secure the bone graft in place.

iliac crests, ascending rostrally in the line with the sacral spinous processes. The vertebrae bisected by this line are termed stable vertebrae. The length and location of the stabilizing construct are critical.The implant length must be sufficient to apply the necessary bending moment to the spine, but it must not be so long that it creates excessive spinal stiffness.The apical and neutral vertebrae in the coronal and sagittal planes must be assessed (Fig.8). An implant should not terminate at or near an apical vertebra.If a long moment arm is extended to, but not above, an apical vertebra, there exists a significant risk for deformity progression (Fig.9). The determination of the apical vertebra is therefore a critical component of the decision making process.Several clinically relevant deformity classification schemes have been developed. KING. et, al.[20] divided coronal plane deformities into five categories for classification of idiopathic scoliosis:Type-I, a double concave curve in which the lumbar curve is larger and more rigid than thoracic curve;Type-II, a double concave curve in the thoracic is more rigid than the lumbar curve; Type-III, a thoracic curve; Type-IV, a long thoracic curve that tilts into the curve and Type-V, a double thoracic curve that tilts into the concavity(Fig.10).The management of these curves depends on curvature type and other patient specific characteristics, In the scheme described by Lenke et,al [23], the position of the lumbar apical vertebra with respect to the central sacral line is strongly emphasized (Fig.11).The compensatory curve forms in response to the primary

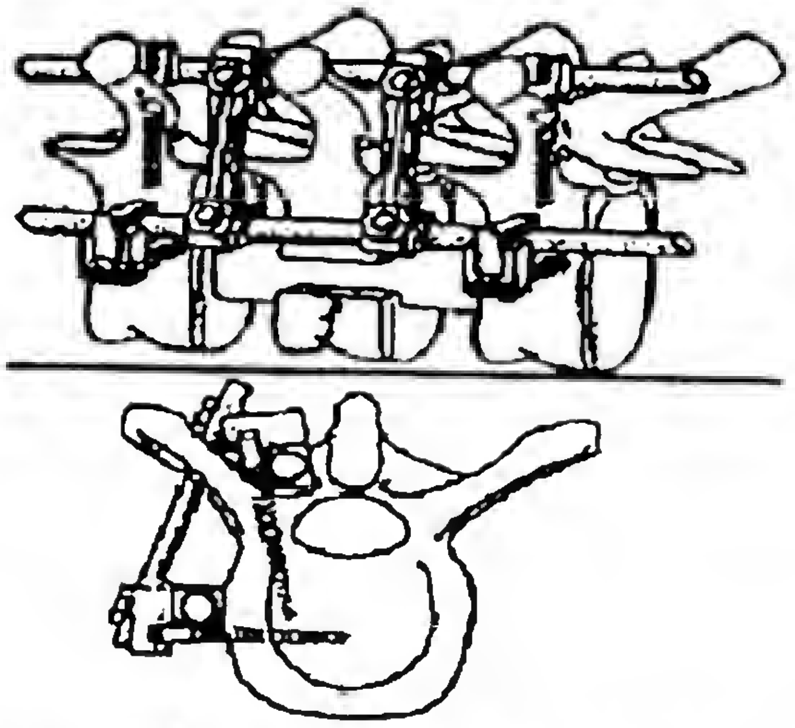

Fig.17. A lateral *(upper)* and axial view *(lower)* of the crossed-screw fixation technique. Note that rigid cross-fixation maintains the near 90° screw toe–in angle.

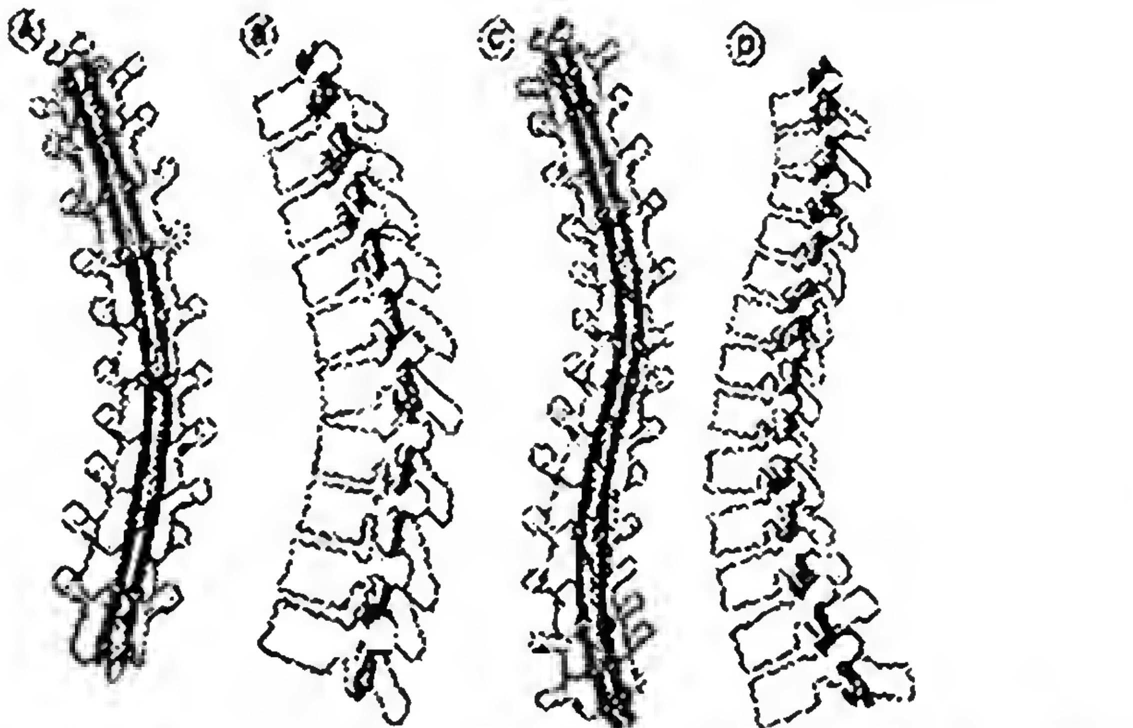

Fig. 18. A: Spinal derotation is achieved by careful simultaneous rotation of two rods attached to the spine in its deformed scoliotic state. B: The rotation of the rods by 90° converts a scoliosis (A) to a kyphosis (B). If the residual kyphotic deformity is unacceptable, it may be corrected by rod contouring. C and D: This strategy can be applied to biconcave curves as well.

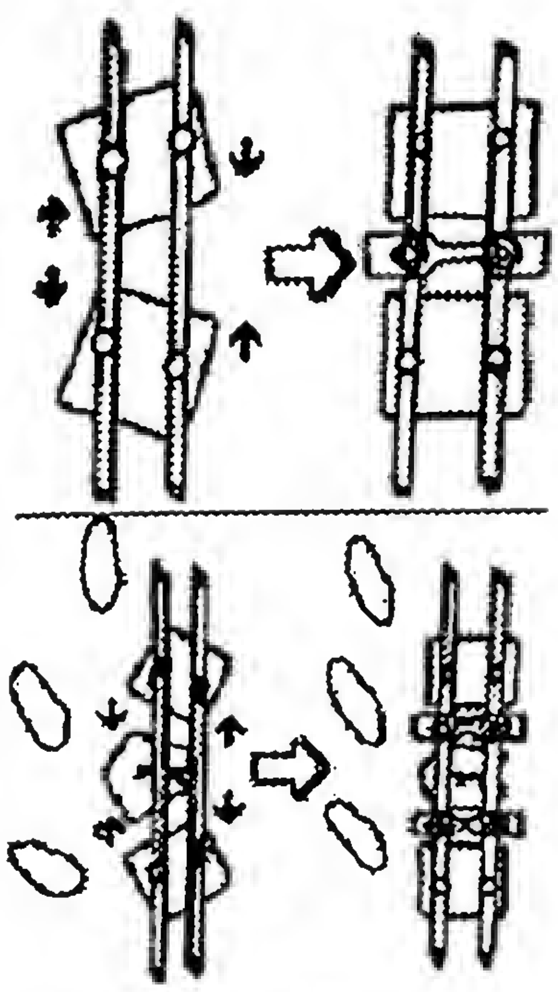

Fig. 19. *Upper:* Intrinsic implant bending moment application. *Upper Left:* In this case, simple distraction of the concave side of the curvature and compression of the convex side achieves the reduction of a scoliotic deformity. *Upper Right:* Cross-fixation is usually used to assist in the maintenance of the reduction. *Lower Left:* In this case, laterally placed transverse VB screws are manipulated (distracted and compressed; *arrows*) to reduce a kyphotic deformity. *Lower Right:* Compression of the two most dorsal screws and distraction of the two most ventral screws achieves reduction of this deformity. Cross-fixation is usually used to assist in the maintenance of the reduction.

curve's reflexive attempt to achieve balance.

Component Strategies For Deformity Prevention And Correction.

Complex deformities can be corrected using spinal implant-induced forces along one axis or a combination of the three axes of the Cartesian coordinate system, by which the spine is brought to the implant (Fig.12). Bending moments applied in the sagittal plane are of three- or four point bending or applied moment arm cantilever beam types. Three point bending force application consists of a fulcrum that directs a force vector contralateral to the direction of the terminal force vectors (Fig.13). In Harrington rod or universal spinal instrumentation application, techniques involve three point bending force application over multiple spinal segments. Dorsally directed forces are applied at the upper and lower termini of the construct and a ventrally directed force is apllied at the fulcrum. This is equal to the sum of the dorsally directed forces. Four point bending force applications involve the loading of a spinal segment with two transverse forces on one side and two on the other. The bending moment is constant between the two intermediate points of force application. The bending moment peaks at the intermediate points of force application with three-point bending and two intermediate points of force application with four point bending construct.

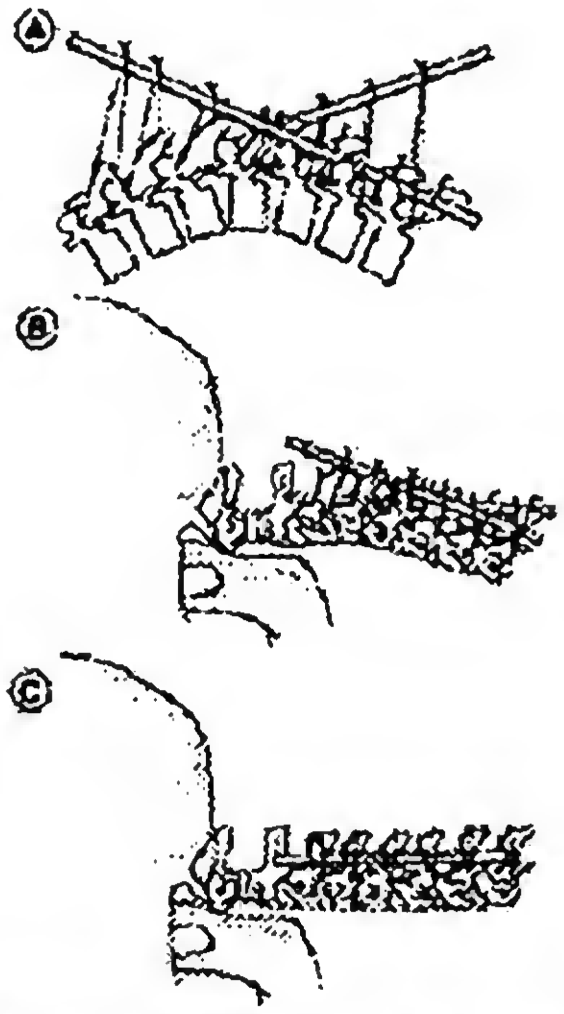

Fig. 20. The crossed-rod technique of three-point bending force application in the cervical spine. This can be applied by rods and screws or, as depicted, by rods and wires or cables.

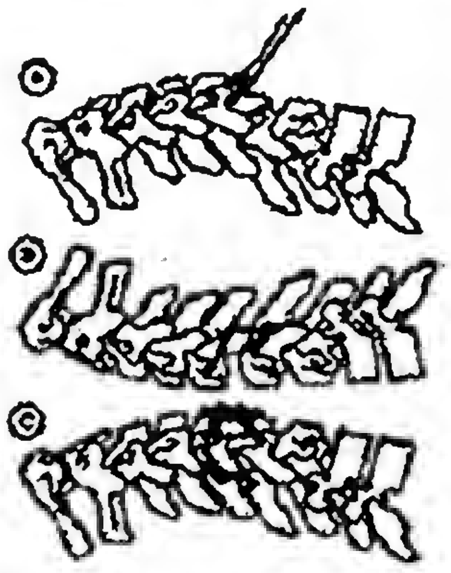

Fig. 22. A 540° operation is occasionally indicated. Ventral decompression (A), followed by a dorsal reduction (B), and ventral stabilization and fusion (C) may be used to decompress, reduce, and stabilize the spine, respectively.

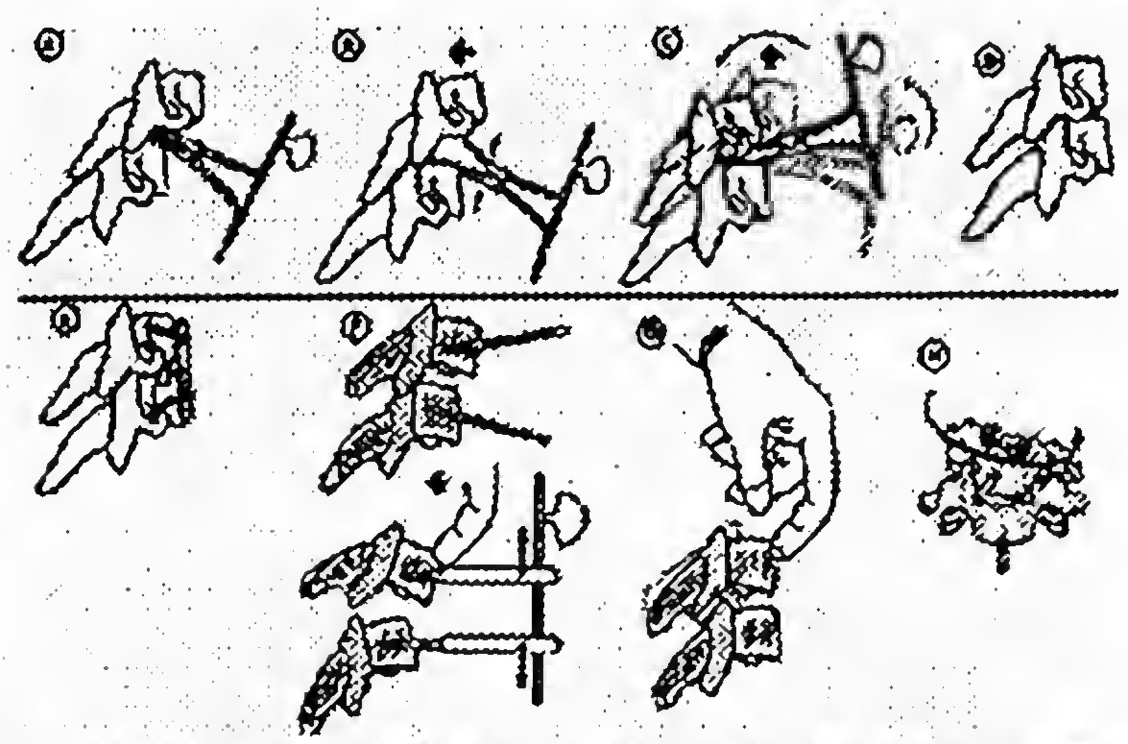

Fig. 21. The management of a cervical dislocation with locked facet joint(s) via a ventral approach. After a decompressive discectomy (A) to release/relax the spine, distraction can be performed using a disc interspace spreader (B). This disengages the locked facet joints. Dorsal rotation and relaxation of the applied forces (after the facets have been "unlocked") results in the resumption of the normal spine posture (C and D). Fixation and fusion in normal alignment may then be achieved (E). Caspar pins and distractors can also be used. Pins placed in an angular orientation can be used to exaggerate a kyphosis to disengage the facet joints (F), thus permitting reduction (G). Removal of the distractor and pins then restores normal alignment. Rotational deformity, such as that which occurs with a unilateral locked facet, can be reduced by placing Caspar pins out of the midsagittal plane (H).

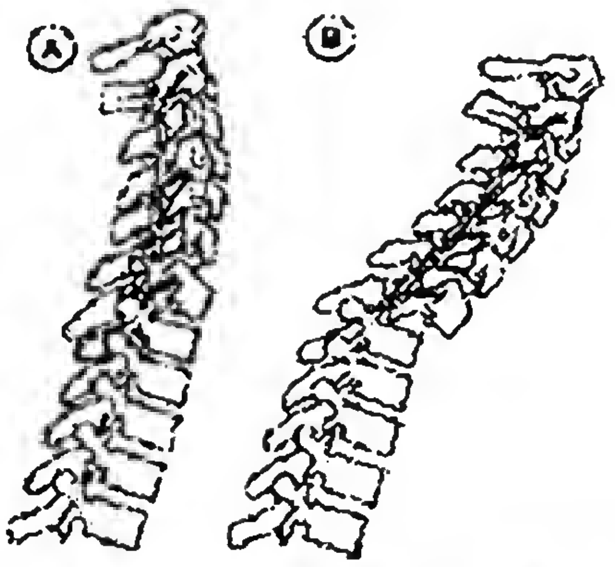

Fig. 23. A: A long implant should perhaps not terminate at the cervicothoracic junction. B: Should this occur, the deformity may become exaggerated at the terminus of the implant.

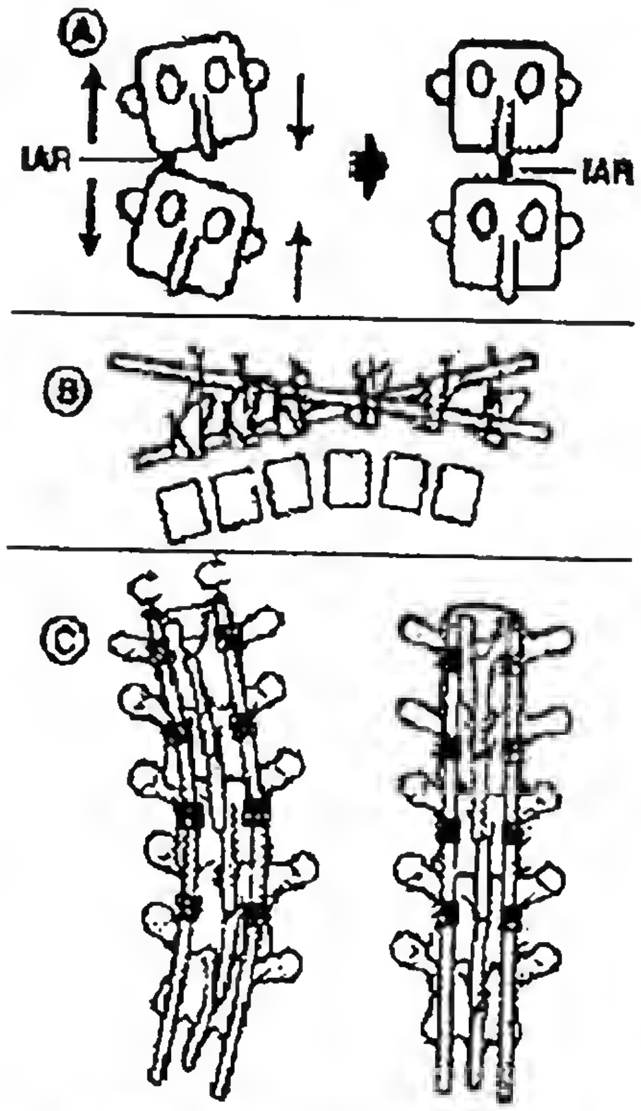

Fig. 24. Coronal-plane deformities may be reduced using compression and distraction (A), the crossed-rod technique (B), the derotation maneuver (C), or a combination of these techniques.

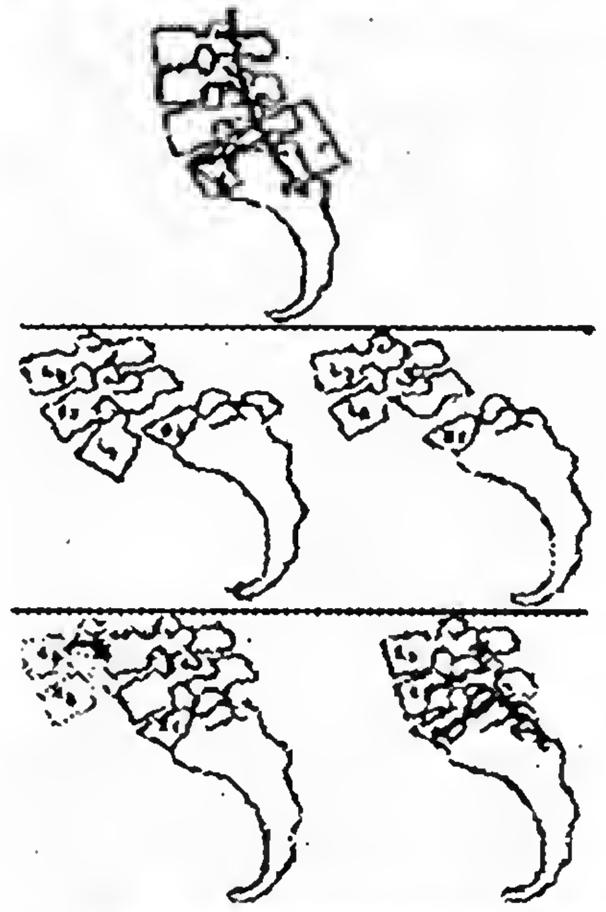

Fig. 25. *Upper:* Long moment arms (d and d') that pass ventral or caudal to the lumbosacral pivot point *(dot)* can apply adequate leverage for deformity correction and prevention. An L5–S1 spondylolisthesis *(center left)* can be managed by performing an L5 corpectomy *(center right)* and a reduction and the docking of L-4 on S-1 *(lower left)*. An interbody fusion may be used as a spacer and for fusion acquisition. Dorsal instrumentation maintains fixation *(lower right)*. Care must be taken to ensure that adequate room is provided for both nerve roots at the new L4-S1 juncture.

An established technique for the correction of thoracic and lumbar kyphotic deformities is the crossed-rod technique (Fig.14), which was first performed in the Harrington rod distraction. With subsequent use of Luque sublaminar-wires, however, gradual reduction of kyphosis can be achieved by sequentially bringing the spine toward the rod [14] (Fig.15). With sequential hook insertion, universal spinal instrumentation systems may also facilitate application of the crossed rod technique [7].

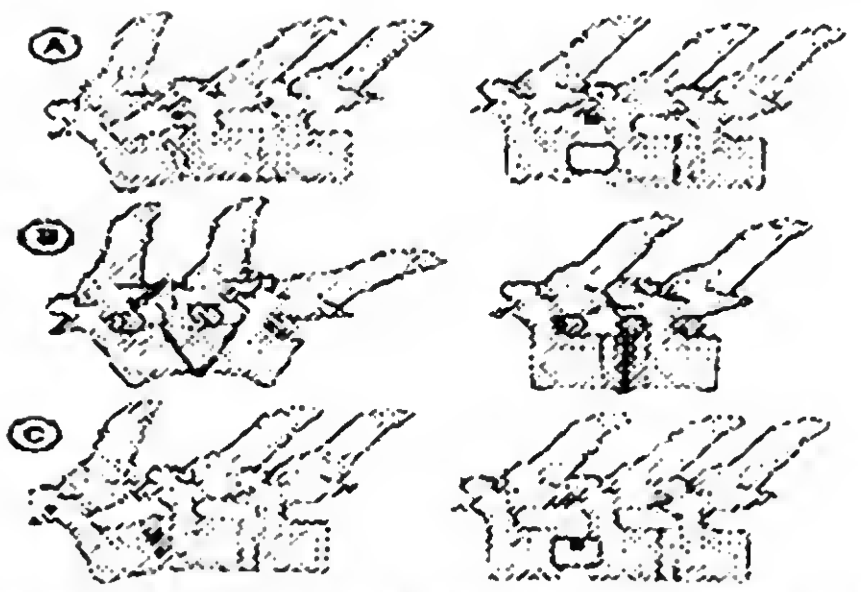

Fig. 26. The axis for sagittal-plane correction is perpendicular to the long axis of the spinal axis (dot in the lateral view). This axis may be located in the region of the spinal canal (A). It may also be located ventrally, in the region of the anterior longitudinal ligament (for example, for dorsal wedge osteotomies (B) or in the middle column region (C))

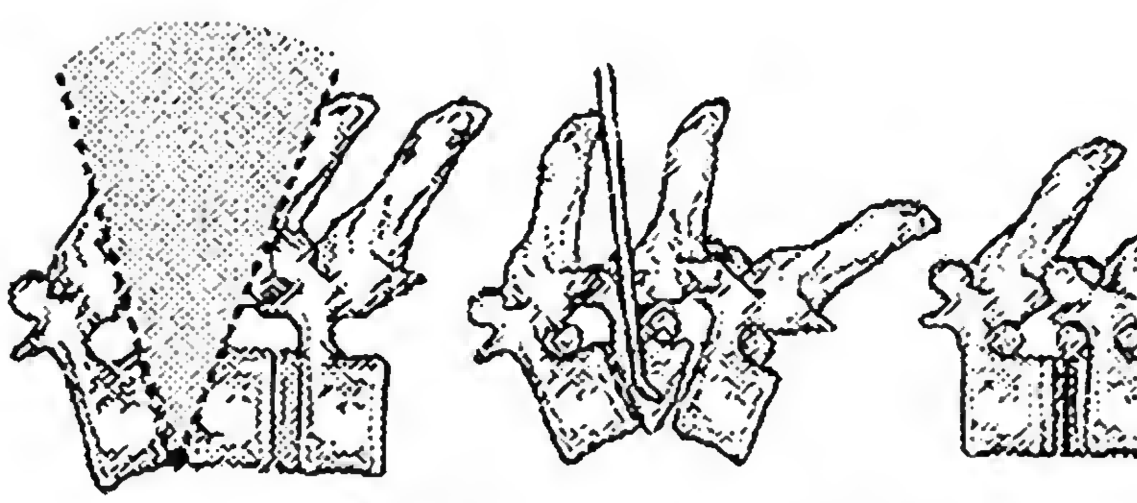

Fig. 27. *Left:* Dorsal osteotomy *Center* and *Right:* Egg-shell osteotomy

IN VIVO ALTERARION OF IMPLANT CONFIGURATION.

Applied moment arm cantilever beam force application.

For short segment fixation,applied moment arm cantilever beam constructs may be placed to reduce the curvature [13,32]. Commonly applied in the thoracolumbar and lumbar regions for deformity correction in cases involving burst and wedge fractures, these constructs require significant loads to be placed at the time of correction. Sagittal plane applied moment arm cantilever beam forces may be applied in either flexion or extension. An applied moment arm cantilever involving distraction and extension may be prone to failure if the implant is excessively loaded [25]. Because interbody strut loading significantly unloads the axial forces through the spinal implant, the risk of hardware failure and progressive deformity is reduced. The procedure involving the sequential application of distraction forces (load bearing), decompression of the dural sac, placement of an interbody strut, and finally compression of the strut is deemed a load- bearing-to-load-sharing force application.

Reduction of short segment parallelogram deformity.

Lateral translational deformities may be surgically treated using the technique of short segment parallelogram reduction. This technique is used when treating lateral translational deformities. In it, a rigid cantilever beam pedicle fixation is performed in the thoracic and lumbar regions (Fig.16). pedicle screws are first placed and rods are applied to friction-glide tightness.Rod holders are subsequently placed and torque applied to both rods simultaneously until fraction reduction is achieved. Rigid cross-rod fixation maintains the achieved reduction. Placement of structural bone graft is then followed by placing screws in compression mode to achieve load sharing.

Crossed screw fixation.

The crossed screw fixation technique requires an extracavitary approach [6] .It can be used to alter sagittal plane abnormalities as an alternative to other short segment fixation techniques. It requires two large VB screws that bear axial loads and two ipsilateral smaller pedicle screws that attain reduction and prevent flexion or extension deformities. The mean 90degrees screw toe-in angle provides rigid cross-fixation (Fig.17). Compression or distraction of the pedicle screw addresses sagittal-plane deformities. Coronal plane angles may be changed by manipulating VB screw relationships. This technique in the purest sense is seldom used.Its underlying principles, however, may often find utility.

In Vivo Implant contouring.

To achieve reduction of a spinal deformity, in vivo implant contouring to alter segmental relationship is often effective. After the placement of pedicle screws or hooks, the rods are fit to the shape of spine. Subsequent in vivo contouring of the rods, with the attached spine, may be used to reduce the deformity. This technique applies unknown and perhaps excessive forces to the spine. Alteration of the relationship between the spine and the implant may occur, such that the screw or hook is overtightened or becomes loosened and then migrates. Sublaminar hooks may be inadvertently forced ventrally, impinging the thecal sac and spinal cord.

Spinal Derotation.

Is performed by careful rotation of two rods that have been attached to the spine in its deformed scoliotic state [11]. The 90 deg.rotation of the rods can be used to convert a scoliotic to a kyphotic curve (Fig.18). If the resultant kyphotic deformity is unacceptable, it may be corrected by contouring the rod. Biconcave curves may also be corrected in this manner. These maneuvers must be performed gradually to allow for continuous assessment of the implant-bone and component-component relationships. If the hooks do not rotate with the rod, significant stress at the hook-bone interface may occur. Suboptimally placed pedicle screws may cut out during rod rotation.

Intrinsic Implant Bending Moment Application In The Saggital Or Coronal Plane.

After placement of screws and loosely connected rods, correction of a scoliotic curve may be achieved by distraction on the concave side of the curve with simultaneous distraction on the convex side (Fig.19). This technique may be performed to correct both coronal and sagittal plane deformities. Care should be taken to achieve friction-glide tightness at the interface prior to distraction so that the screws maintain their angular relationship with the rod during distraction.

Maintenance Of Deformity correction.

Cross fixation of bilaterally placed rods substantially augments the integrity of the construct [12,14,26]. If the maintenance of deformity correction depends on cross connection, as in cases of short segment parallelogram deformity reduction, the use of cross fixation in short constructs is essential. Longer constructs involving cross fixation provide a quadrilateral frame construct that offers increased rotatory and torsional stability. Cross fixation also enables maintenance of the desired interrod width, which may prevent hook migration or screw dislodgment. Screw triangulation plays an integral part in the prevention of lateral translational deformation. Screw toe in may be used in conjunction with cross fixation to allow, in a "Belt and suspender like" manner, the corrected curvature to be maintained.

REGION SPECIFIC STRATEGIES:

The various regions of the spine have unique anatomical and biomechanical properties. Thus, is appropriate to consider correction related strategies based on the spinal region.

Craniocervical junction and Upper Cervical Spine.

The high degree of mobility of the CCJ and upper cervical spine leave it vulnerable to deformities in the coronal, sagittal and axial planes. Although many cases may be corrected by non-operative means deformity reduction and occipitocervical fusion are occasionally required. Angular bending moment application, which resists rotation of this region, may be required. This may be addressed by the technique of Occipito-Cervical fusion or transarticular C1-2 screw fixation.

Lower Cervical Spine.

Deformity correction in this region presents unique regional challenges. The ease of ventral and dorsal exposure is offset by relatively poor availability of adequate fixation points, especially dorsally.

Coronal Plane deformities.

Cervical scoliosis is an uncommon entity.The application of concave distraction and convex compression, as well as the use of the derotation maneuver, may be used to correct such curves. The recent introduction of rod and screw constructs has facilitated the use of these techniques.

Sagittal Plane deformities.

Are relatively common and consist of kyphosis and spondylolisthesis. The degenerative changes of the cervical spine frequently alter normal cervical lordosis. This usually starts with loss of disc space height and follows with subsidence of the cervical vertebral bodies. The moment arm substantially increases as kyphosis worsens, and this promotes further deformity, and progression of this deformity may be further complicated by progressive myelopathy. Ventral, dorsal or combined approaches can all be used in cervical kyphosis. Ventral approach provides direct decompression of ventral lesions, while allowing kyphosis to be corrected by placing a strut graft, and also can be performed to release the anterior cervical spine to decrease forces placed during second stage correction of the dorsal deformity. Several dorsal techniques may also be performed to reduce cervical kyphosis. The crossed rod technique, enhanced by ventral release, may be conducted (Fig.20), and can be applied via lateral mass screw fixation. Weakening or disrupting the dorsal tension band tends to exaggerate sagittal plane deformations. Fusion may be indicated in selected patients at risk for post-laminectomy kyphosis. Laminoplasty may decrease the risk of post operative deformity by minimally disrupting the dorsal tension band. Cervical translational deformities like trauma induced subluxation may result from flexion distraction force applications, which may result in facet dislocation.Ventral decompressive surgery followed by reduction [8,27] . is preffered .

Distraction of the disc interspace may disengage the locked facet joints, allowing for stabilization and fusion in a single stage procedure (Fig.21) .Dorsal reduction and fusion must often begin with partial resection of the facet joint.This iatrogenic destabilization, by removal of the facet joint may obligate the incorporation of an additional motion segment into the fusion. In certain cases, a failed initial attempt at ventral reduction may require a combined ventral-dorsal-ventral approach (540 deg), which provides ventral decompression and both ventral and dorsal stabilization (Fig.22).

Cervico-Thoracic Junction.

Biomechanically , the transition from a cervical lordosis to thoracic kyphosis and a shift from the mobile cervical spine to the far less mobile thoracic spine represents a major transition in kinematics, thus makes this region challenging to manage and a unique region of the spine. Decompression of this junction via a dorsal approach may often necessitate dorsal fusion to prevent the development of deformity. Long implants should not terminate at this junction but should extent through the transitional zone (Fig.23).

THORACIC SPINE.

Is characterized by larger VBs that are protected by rib cage and a relatively smooth bend at each segmental level. Deformities often have elements in each of three fundamental planes. Scoliosis is a complex deformation that is nearly always associated with the phenomenon of coupling. This occurs when one deformation along or around an axis obligates a second deformation along or around the long axis of the spine. Thoracic scoliotic deformities rotate the spinous processes towards the concave side of the curve, resulting in axial load forces transmitted on the concave facet joints. This is usually associated with loss of thoracic kyphosis. Correction of the curvature may often require a ventral release to achieve adequate correction. Surgical release procedures are usually combined with ventral interbody fusions.

Coronal plane deformities.

May be corrected via ventral, dorsal, or combined approaches. In the pediatric population, skeletal maturation must be appreciated. In the skeletally immature patient a stand alone dorsal approach may result in unopposed ventral growth (crank-shaft phenomenon). Ventral strategies typically involve segmental screws and rods placed on the convex side of the curve from neutral to neutral vertebra. The result is typically a shorter construct than that achieved dorsally. Compression and distraction, , derotation oracombination of strategies are conducted to reduce thoracic deformities via a ventral approach (Fig.24).Ventral procedures tend to promote kyphosis more than the dorsal procedures involving constructs. Dorsal procedures involve similar maneuvers to achieve correction. Scoliosis correction achieved using dorsal derotation methods requires longer constructs and is usually supplemented by concave distraction and convex compression [9] . Longer constructs often lead to higher incidence of rod fracture and acceleration of end fusion degenerative changes. Strategies to combat these include cross-fixation, larger diameter rods, and external immobilization [19] . The use of pedicle screw fixation may limit the length of the construct required.

Sagittal Plane deformities.

The first step in correcting a kyphotic deformity is its objective assessment. This may be accomplished by measuring the angle from the superior endplate of the VB one level above the involved VB to the inferior endplate of the VB below. The correction itself begins by undertaking the crossed rod procedure, which is supplemented with ventral interbody distraction as necessary (Fig.15). Longer constructs are generally more effective because of the larger bending moment that can be generated through the longer moment arm. In situ, rod bending can also be performed to make final adjustments, but this places additional stresses on the implant,as well as the spine.

THORACOLUMBAR JUNCTION.

Is a transitional zone of the spine. The aforementioned strategies for coronal and sagittal plane deformities in the thoracic region may be similarly applied to this region. Ventral release procedures,via open or endoscopic techniques, combined with interbody structural struts, may substantially facilitate deformity reduction and the maintenance of correction [31] . Coronal plane deformities spanning the T-L junction often require long dorsal fixation. These deformities are typically complex, often comprising two or more curvatures. If the fusion extends to the level of L-4 and below, motion will be significantly affected. Coronal plane balance, which may be assessed by using CSL, must not be overlooked.

LUMBAR SPINE.

The above mentioned strategies for the thoracic and thoracolumbar spine are likewise applicable to the lumbar spine. The majority of deformities have a significant translation component that requires careful consideration of sagittal plane balance. An important factor in the attainment and maintenance of lordosis is intra-operative positioning. Surgical beds or frames that facilitate lordosis by encouraging extension of the spine and hips are optimal. Intra-operative pelvic flexion can result in inadequate lordosis with a resultant flat back. The sagittal vertebral axis should be brought back to the dorsal L5-S2 joint, which may require aggressive osteotomy and / or ventral load bearing adjuncts.

LUMBOSACRAL REGION.

Poses unique and complex biomechanical challenges. Instability may be assessed by examining flexion and extension radiographs. Whereas they are commonly obtained while the patient is standing, the lateral decubitus position off loads the spine, thus minimizing pain and allowing a more accurate assessment. Spondylolisthesis may require aggressive surgical strategies and accompanying lumbar, sacral and pelvic fixation. The likelihood of deformity progression must be known. Patients in whom the degenerative process has begun are less likely to slip further than those in whom it has yet to begun. Partial correction is often obtained after positioning. Three point bending force application may facilitate reduction by pulling back the intermediate (L-5) screw of a three screw construct. Long moment arms that pass ventral or caudal to the lumbosacral pivot point are often required to achieve adequate correctional bending moments (Fig.25). Although complete deformity correction is the goal, it is often difficult .

Ventral and Dorsal Osteotomy.

A variety of ventral and dorsal osteotomy types may help to achieve deformity correction. When considering the usefulness of osteotomy-induced correction, two factors are important: extent of correction required and degree of ankylosis. The axis around which the correction is to be achieved must be considered (Fig.26). The goal of deformity correction via osteotomy is to shift the sagittal axis dorsally, bringing the spine into balance. Regardless of the type of osteotomy performed, it is most effective when performed at the apex of a curve. Dorsal osteotomy is most safely performed in lumbar spine, where the disc interspace and pedicles have been removed. The axis of rotation is around the anterior longitudinal ligament (Fig.27).

CONCLUSION.

The correction of deformity may be achieved by a variety of methods, each with advantages and disadvantages. Understanding the biomechanical principles involved facilitates the clinical decision making process, thus enabling the surgeon to optimize patient outcome. The ultimate goal is to ensure a biomechanically sound environment, and facilitate a non- pathological relationship between the neural elements and the surrounding osseous and soft tissue confines.

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SMOKING AND KIDNEY

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Cigarette smoking is injurious to health – a notion is written on all cigarette packs. Inspite of that people love to enjoy the taste and flavour of every puff of it. Because of change in life style and adoption of western cultures rapidly by the developing countries, a double fold increase in the incidence and prevalence of smoking in last few years with more involvement of female gender. Its negative impact on multiple organs has forced the investigators to label smoking as a component of category 1 modifiable risk factor for many organ system diseases.

Apart from the adverse effect of smoking on heart, lung, stomach, blood vessels, it is a factor in the development of cancer, hypertension, preeclampsia and eclampsia, Kidney is also an important target organ of smoking induced damage. Although 19th and 20th centuries noted an association between smoking and renal' it was in 1997 only that the neprologists rediscovered smoking as a major renal risk factor.[2]

Acute and chronic smoking has been documented to be associated with renal function impairment, probably mediated by smoking induced changes in vasoactive hormones. Cross sectional and longitudinal studies have shown that smoking has an adverse effect on one in general population, essential hypertension, primary and secondary ; renal vasculature; graft and patient survival in renal transplant recipients and diabetic renal diseases.

Histologic features of smoking induced Renal Damage

Compared with non-smokers, smokers exhibited more severe myointimalsia of intrarenal arterioles' more particularly evident in patients >50 yrs. of age. More severe glomerulosclerosis and tubulo interstitial fibrosis has been documented" and an increase glomerular basement width in patients with type 2DM who smoke has been preliminary biopsy study[5].

Potential Mechanism of Smoking Induced Renal Damage

Several potential mechanisms of smoking induced renal damage joind been but the precise nature of the nephrotoxic effect of smoking is not well known Various pathomechanisms causing renal damage can be acute particularly 1) sympathetic activation (influencing BP and renal hemodynamics) or chronic particularly cell dysfunction (diminished Nitric oxide availability, diminished endothelial dent vasodilation and intimal cell hyperplasia). Smoking causes a transient increase BP and heart rate (app. 30mts.) and alters the diurinal rhythm of BP[7]. Smoking also causes alterations of intrarenal hemodynamics particularly a decrease in renal plasma flow as a result of renal vasoconstriction. A genetic approach to explain the different susceptibility of individuals to induced organ damage has been proposed by Wang et al[9]. In this context, BENEDICT (Bergamo Nephrologic Diabetes Complications Trial) is noteworthy. A genetic predisposition of smokers to develop albuminuria was found in carriers of the DD-of the ACE gene[10].

Smoking and Various Kidney diseases

In general population, smoking increases urinary albumin/protein excretion rate (AER/PER) and increases the risk for renal functional deterioration especially in men and in elderly. Hillege HL[11]; Pinto Sietsma SJ et al[12]; Halimi JM et al[13]; in separate studies noted that the albumin excretion rate was correlated with the number of cigarettes with men smoking more than 20 cigarettes per day at double the risk than those smoking more than 20 cig./day. Similarly, dose dependent increase of the relative risk of end failure (ESRF) was found in smokers as compared with non-smokers in Multiple Intervention trial(MRFIT).[14]

In Patients with Primary Hypertension, prevalence of microalbuminuria is almost double in smoking than non-smoking lean patients". HOPE study' and a recent study" patients with hypertension and left ventricular hypertrophy smoking > 20 /day had a 1.6 fold higher prevalence of microalbuminum and a 3.7 fold higher of macroalbuminuria than non smokers. However, an effect of smoking on renal functional deterioration is controversial and at this point of time generalization effect of smoking on ESRF is primary hypertensive patients cannot be documented.

In diabetic nephropathies, Christiansen[18] and subsequently Telmer et al[19] in a large series study found an increased frequency of nephropathy with about 13% in patients who smoked <10 cigarettes /day and > 25% in patients who smoked 30 cigarettes/day. Available documents the increased risk of microalbuminuria; accelerated rate of

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progression from microalbuminuria to manifest proteinuria2[0] and accelerated progression of renal failure[21] in smokers with type 1 as well as type 2 diabetes mellitus.

In nondiabetic patients with establish primary renal disease involving kidneys, there is no pertinent evidence in the literature of their higher involvement in smokers.[22] However, solid evidence has accumulated that smoking is a major renal risk factor in patients with establish primary renal disease as a ADPKD, IgA glomerulonephritis[24]; chronic glomerulonephritis and in systemic disease involving the in lupus nephritis; Pauci immune ANCA positive extracapillary nephritis and Good Pastures syndrome.

Prevelence of peripheral vascular disease (PVD) is higher in smokers and as renal is higher in PVD patients it is not surprising that smokers have a higher risk of critical atherosclerotic renal artery stenosis[28]. Smoking narrows the lumen of renal as well as increases the incidence of cholesterol microembolism[29] thereby making it necessary all patients with extra renal atherosclerosis who continue smoking, to detect early ischaemic nephropathy.

In contrary to previous report, recent prospective study provides solid evidence for an effect of smoking on graft function[30]. Effect of smoking on renal allograft function may depend on renal disease that has led to ESRF. e.g. in patients who had reached ESRF as result of Lupus nephritis, the risk of renal transplant loss was substantially higher in smokers.

Management

The best management is to quit smoking and major efforts include;

i) Awareness about various negative side effects of smoking.
ii) Psychological support
iii) Counseling therapy
iv) Effective pharmaceutical smoking cessation approaches i.e. Bupropion and Nicotine replacement therapy.

However, to date controlled information on the success of modern smoking cessation in renal patients is not available.

Inspite of the damage done to multiple organ systems doctors always advise to quite smoking. The question is what is the renal benefit derived from smoking cessation? In patients with type 1 DM and non-diabetic nephropathies, the risk of microalbuminuria was only minor in ex-smokers, but significant in current smokers.

At present no date is convincing and does not allow for the drawing of definite conclusion about the magnitude of renal benefit derived from smoking cessation. When the above data and clear negative impact of smoking on renal function in patients with renal disease is taken into account, it is rational to conclude that smoking cessation is one of the single most efective measures to retard progression of renal failure – quite apart &om its undoubtedly from beneficial effect on cardiovascular risk[31].

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CHANGING SOCIODEMOGRAPHIC AND CLINICAL PROFILE OF SUBSTANCE USE DISORDER PATIENTS IN KASHMIR VALLEY

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***Abstract**: Psychoactive substance use is an increasing public health concern. Although levels of illicit substance use in many developed countries had remained stable or even declined for a number of years, the patterns of use now appear to be changing. . There is also increase in use of opioids, cocaine and other psychotrophic substances in developing countries. This trend is also worsening in Kashmir valley over the last few years. The present study compared the substance abuse in 1980-88 and 2002 in patients presenting to the psychiatric disease hospital. There has been an alarming increase in the use of opioid-based preparations (9.5% to 73.61%) along with multiple substance use (15.8% to 41.6%)from 80's to the year 2002 respectively. Pattern of abuse has also changed in female patients. Among the various reasons for substance abuse significant number attributed it to the prevailing condition in the valley (11%). Other findings are discussed in the paper.*

***Key Words**: Substance abuse , Kashmir , changing pattern,*

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Introduction

Addictive disorders are among the worlds leading public health problems and cause enormous human suffering, cost and threaten the very social fabric of many communities around the world[1]. Last few years have seen phenomenal increase in mental morbidity in Kashmir (2) Substance use disorders as reflected in the out patient department (OPD) patient population of the sole psychiatric disease hospital of Kashmir valley has also shown a substantial increase (3). Like most social behaviors the etiology of substance abuse is complex varying through time, geographical regions and by demographic characteristics[4]. Many developing countries have seen rapid increases in the use of opioids, cocaine and psychotropic drugs, and resulting problems. In a number of these countries drug injection is becoming increasingly common. (5) In the recent past certain disturbing trends have been observed in the valley. The abuse of the traditionally used drugs is being replaced by harder substances like heroin and over the counter drugs like opiates, injections like pentozocaine , morphine, combinations of injections like pentozocaine diazepam , promethazine ,codeine containing cough syrups and preparations containing dextropropoxyphane , diphenoxlate ,buprenorphine and benzodiazepine . Keeping these emerging trends it was decided to compare the pattern of drug use disorders attending the sole psychiatric diseases hospital OPD in 1980's with 2002.

Material and Method

This study was conducted at the hospital for psychiatric disease Srinagar from March 2002 to November 2002. All the patients between age group of 16-60 years attending the out patient department (OPD) of the hospital from march 2002-november2002 for any substance use disorder including substance abuse, dependence, intoxication, withdrawal, substance induced disorder were selected for the study. The exclusion criteria included non-availability of consent, age below 16 and above 60, patients with organic brain disorder, Patients with medical condition like hypothyroidism, hyperthyroidism, pheochromocytoma, Cushing's disease etc. A total of 72 subjects fulfilled the criteria for the study.

The subjects were interviewed in detail in the psychiatric disease hospital. They were requested to provide all the requisite sociodemographic information and divulge complete drug use history, which was followed by a detailed psychiatric examination.

The American psychiatric associations diagnostic and statistical manual 4th edition (DSM IV) criteria were used

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to diagnose substance use disorders.

RESULTS

72 patients with drug use related problems attended the out patient department of the hospital from March2002 to November 2002

Table I: Socio demographic and clinical variables

	Jan Dec 1980- 1988	March-Nov2002
Total no of patients	189	72
Males	99.5%(188)	97.2%(70)
Females	0.5%(1)	2.8%(2)
Urban	57.14%(108)	54.16(39)
Rural	42.86%(81)	45.84%(33)
Married	51.9%(98)	56.94%(41)
Unmarried/separated	48.1%(91)	43.05%(31)
Primary Drug Of Abuse		
Cannabis	77.8%(147)	16.66%(12)
Opiods and related	9.5%(18)	73.61%(53)
Alcohol	4.8%(9)	9.72%(7)
Multiple substances	15.8%(30)	41.66%(30)
Duration of Abuse		
Less than 1 year	3.17%(6)	6.94%(5)
More than 5 years	35.97%(68)	41.66%(30)
Referral		
Self referral	14.81%(28)	13.88%(10)
Private clinic	7.93%(15)	59.72%(43)
Education		
Beyond 10th class	16.40%(31)	37.5%(27)
Graduated	10.04%(19)	20.83%(15)
Initiation of substance use		
Peer group pressure	72.48%(137)	44.44%(32)
Curiosity	8.99%(17)	16.66%(12)
Family Discord	11.1%(21)	11.11%(8)
Prevailing conditions	—	11.11%(8)
Failure in love affair	7.4%(14)	8.33%(6)

Discussion and Conclusion

Although the findings of the study do not show much change in the socio demographic variables in 1980's and year 2002 but some findings are still striking and reflect the disturbing trend. While as the only female addict in the whole sample of 1980's was in her late 60's and only addicted to traditionally abused very small quantity of raw opium, both the women in the 2002 year sample were in their late 20's and had been abusing multiple over the counter available psychoactive substances. One of the females from rural back ground and educated up to primary level only besides consuming 10-20 dextropropoxyphane and 10-20 tablets alprozolam was injecting herself 5-10 ampoules of pentozocaine almost daily for more than a year.

Table I shows the changing pattern in the nature of the primary drug abused by the addicts in the two groups. Whereas the cannabis was the commonest (77.8%)substance abused during the 80's only small %age (16.6%)abused it as a primary drug of abuse in 2002. This finding also reflects the erosion of the traditional patterns of substance use in Kashmir society. As reported in the earlier studies the tradition of cannabis (charas) intake has thrived in Kashmir till recent past in the shape of *charas takiyas* (dens of charas addicts) (6)

Heroin abuse that started in mid 80' in Kashmir (2) is the commonest (73.61%)substance in the sample of 2002. This reflects a very alarming trend. The dangerous dimension of this development becomes all the more frightening when viewed in the light of the media reports that Jammu border becoming the main transit point of international heroin smuggling from the golden crescent (7). Out of the three regions of the state the socio cultural milieu including the culture of *charas takias* makes the valley the most vulnerable region for heroin abuse as has already been revealed by one of our earlier studies (2) The alcohol abuse has continued to be abused least when compared with the other states for the obvious reason that alcohol has never been a socially approved beverage in the valley in contrary to Jammu or other parts of northern India(8). Equally disturbing finding of this study is the increase in multiple substance use (41.6%) in 2002 when compared with only 15.8% drug 80's (2)

The other findings of the study revealed that the majority of the patients belong to the lower socioeconomic class with mostly educated youth above 10th standard pointing towards unemployed and job related stress to be one of the possible reason for substance use. Duration of abuse was more than 5 years in most of the sample pointing towards the chronicity of the problem lack of treatment services in the community. Most of the patients were referred from private clinic by the first author (MAM) showing the reluctance of the patients to come directly to a highly stigmatized place for treatment of such disturbances on one hand and lack of separate de-addiction facilities on the other. One of our earlier studies comparing the treatment follow up results clearly indicted that the results were much better (56.96%) in the drug de addiction center than the general psychiatric hospital (18.8%) (9)

Like the previous study peer group pressure adjustment problem continue to be the single most cause of substance use. The other cause which was not revealed in the previous study and present in the present one was iatrogenic drug abuse in patients particularly from non judicious use of bezodiazipine for various anxiety and depressive disorders with codeine and opiods for pain related disorders which thus merits a serious review within our own community of clinicians. Another disturbing trend has been reference by 11.11% of patients to the present prevailing conditions for the initiation of drug use. More disturbing is the diagnosis of PTSD in these patients thus making the trend more thought provoking because the possible link of stress related disorders and substance use which has alarmingly increased in the valley in the past decade (10,11)

This particular possible association between substance use and PTSD warranted a community based study and has already been undertaken by the first author (MAM).

The limitation of this study has been a hospital-based treatment seeking population possibly different from the community where substance uses is still not thought to be disease but a social or a legal problem only. Drug abuse must be considered a total community problem and thus the responsibility of every one. Harmful effect on health from substance abuse needs in-depth study. Access to availability of addictive substances and its spread needs to be checked with joint efforts of all concerned government agencies, NGO'S at community and individual level. As emphasized in earlier studies also the dread full repercussions of ever increasing drug abuse in the state of Jammu and Kashmir provides sufficient justification for the urgency to evolve and apply preventive, curative and rehabilitative strategies before it is too late.

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CANCERS OF THE UPPER AERODIGESTIVE TRACT IN KASHMIR (A CLINICO-PATHOLOGIC STUDY)

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ABSTRACT: In a clinicopathology based study of upper aerodigestive tract cancers conducted on patients, attending the Department of Otorhinolaryngology & Head & Neck Surgery of S.M.H.S. Hospital of GMC Srinagar from January 2001 to December 2002. 92 patients with cancers of upper aerodigestive tract were managed during this time period the youngest being 6yr old and the eldest 80years old. The squamous cell carcinoma was the commonest histological type accounting for 73% of the cases and the sinonasal tract was the commonest site affected (22%), followed by larynx (19.5%), hypopharynx along with cricopharynx (18%), nasopharynx (14%), oropharynx (10%), salivary glands (9%), and oral cavity (7.5%). Most of the tumors are diagnosed in late T3 / T4 stage except for glottic variety of laryngeal carcinomas most of which are usually diagnosed early in T1 / T2 stage. The clinical symptomatology varied with the site of involvement.

Key Words: Histopathology of cancers, Sinonasal tract, Nasopharynx, Oropharynx, Oral cavity, Hypopharynx, Larynx.

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INTRODUCTION

The upper aerodigestive tract is a mucous membrane lined tract which extends from nares and lips to cricopharynx and glottis and is involved in the important physiological functions like respiration, chewing and swallowing of food and generation and articulation of voice and for obvious reasons the tract is first to be exposed to the inhaled or ingested carcinogens like tobacco, alcohol, occupational dust, nitrosamines and other carcinogens in food. Cancers of the upper aerodigestive tract constitute about 3.5% to 4% of all malignancies.[1,2] These include cancers of the lip, tongue, major salivary glands, gums and adjacent oral cavity, floor of mouth, tonsils, oropharynx, nasopharynx; hypopharynx and other oral regions, nasal cavity and accessory sinuses, middle ear and larynx.[1,2] The major histological type world wide is squamous cell carcinoma (SCC), which comprised 95% of the upper aerodigestive tract cancers in the recent Surveillance, Epidemiology, and End Result (SEER) registries in U.S.A.[1,2,3] In fact larynx and hypopharynx are by far the most common sites of head and neck squamous cell carcinoma.[4] Squamous cell carcinomas of the upper aerodigestive tract has a strong epidemiological background, including racial difference and environmental factors, such as alcohol and tobacco consumption, diet and viral infection; therefore a different pattern of upper aerodigestive tract cancers is expected between the Western and Asian population.[1,2,3,4,5]. We hereby report a clinicopathology based statistics from a single institute in Kashmir.

This study was conducted on patients attending the department of Otorhinolaryngology and Head and Neck surgery of S.M.H.S. Hospital of Government Medical College Srinagar from January 2000 to December 2002. Besides detailed clinical history and routine investigations like complete haemogram, urine examination and kidney function tests, a thorough E.N.T. examination, which included pan-endoscopy, was done in all patients. X-ray chest, X-ray soft tissue neck and C.T scan was done wherever necessary. Biopsy reports were obtained in all the patients.

OBSERVATIONS AND DISCUSSION:-

92 patients with upper aerodigestive tract cancer were diagnosed in this time period with the annual incidence of 6.6 per10,000 hospital attending population. The youngest patient was a 6 year old female with undifferentiated carcinoma of upper gingival region and hard palate and the eldest was 80year old female with squamous cell carcinoma of nose and paranasal sinuses, the average age of presentation was 53.2years, the highest incidence was

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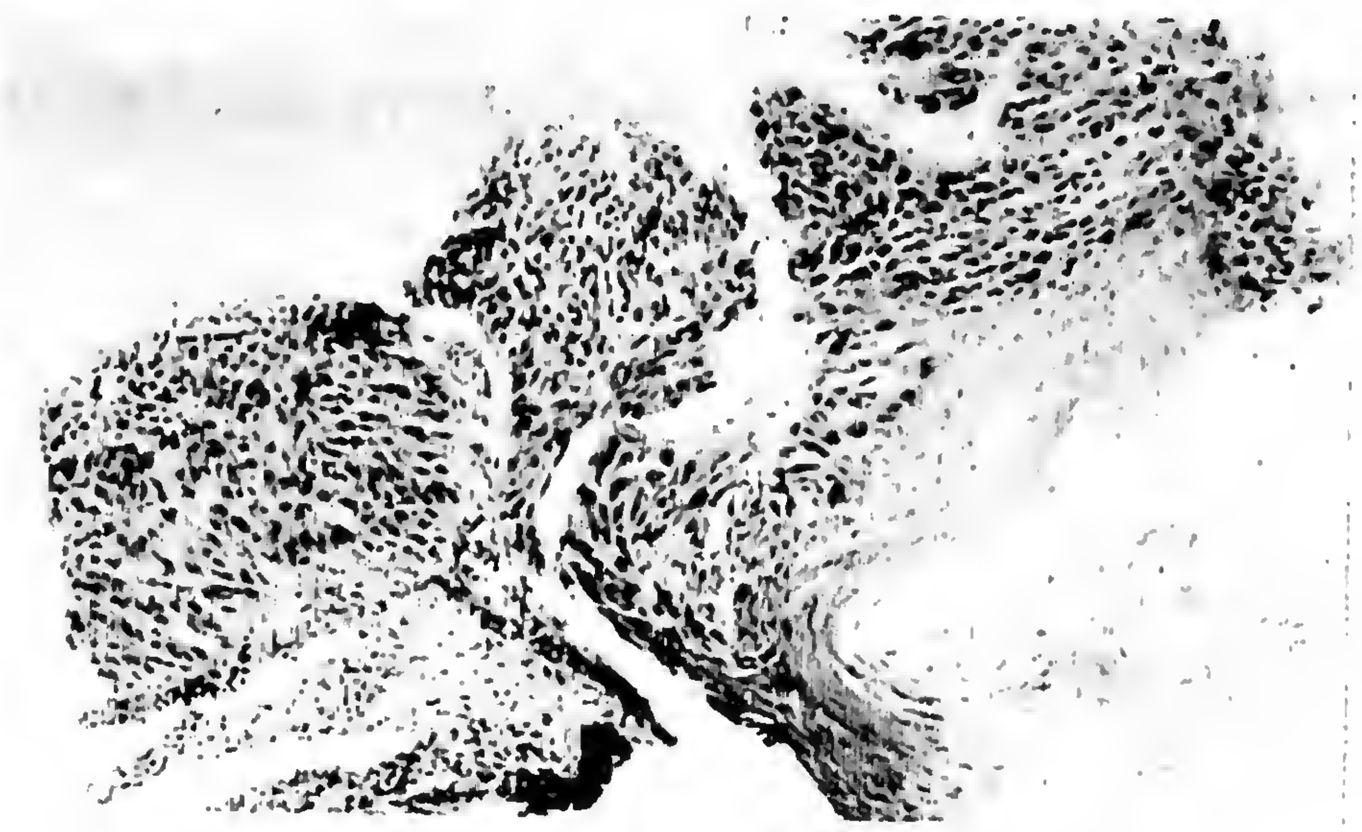

Fig.1: Poorly Differentiated Sqyamous Cell Carcinoma (10x) site: Laryngo-pharynx (hypopharynx).

Fig.2: Non-Hodgkin's Lymphoma (20x) site. Oropharynx.

in the 4th to 6th decade of life and the male: female ratio was 2:1 (table-I.). The commonest symptom of presentation varied with the site of involvement (table-II) and most of the patients presented in latter stages of disease due to lack of health awareness and confusion of the initial symptoms of presentation with the commoner inflammatory and non-neoplastic diseases of the upper aerodigestive tract.

Table-I: Cancers of upper aerodigestive tract: Age and Sex distribution

Age in Years	*Male*	*Female*
0-10	-	1
11-20	-	1
21-30	2	3
31-40	12	4
41-50	18	6
51-60	19	9
61-70	7	4
71-80	2	4
Total	60(65%)	32(35%)

Table-II: Cancers of upper aerodigestive tract: Most common presenting symptoms (in descending order of frequency).

SITE	Most Common symptoms of presentation (frequency)
Sinonasal tract	Nasal obstruction (80%), Epistaxis (60%), Anosmia (30%)
Nasopharynx	Secondaries neck (90%), Nasal obstruction (30%), Otalgia (30%)
Oral cavity	Difficulty chewing (70%), Lesion noticed (60%), 7Secondaries neck(50%)
Oropharynx	Odynophagia (70%), Lesion noticed (50%), Secondaries neck (40%)
Hypopharynx	Odynophagia (70%), Dysphagia (70%), Secondaries neck (50%)
Larynx	Hoarseness of Voice (90%), Secondaries neck (20%)
Major salivary gland	Swelling noticed by the patient (80%), Pain (30%).

90% of the cancers were epithelial in origin and only 10% non-epithelial, with squamous cell carcinoma being the commonest accounting for 73% of the total and 81% of the epithelial variety, Non-Hodgkin lymphoma was the commonest in the non-epithelial variety and accounted for 9% of total this is in accordance with the reports from the other parts of the world.[1,2,3,5,8] Among 92-patients, 67 were with squamous cell carcinoma, 8 with Non-Hodgkin Lymphoma, 5 with Adenocarcinoma, 3 with Adenoid cystic carcinoma, 3 with Mucoepidermoid carcinoma, 2 with Undifferentiated carcinomas, 2 with Melanoma, 1 with Sarcoma (chondrosarcoma) and 1 with Chordoma nasopharynx. (Table-III)(Fig-1& 2)

Table-III: Upper aerodigestive tract cancers: Histological type Distribution.

CATEGORIES	SITE NPNS	Npx	Opx	OC	Hpx	Lx	Sg.	Total
Squamous cell carcinoma	9	12	4	6	16	18	2	67(73%)
Lymphomas	3		5	-	-	-	-	8(9%)
Adenocarcinoma	3	-	-	-	-	-	2	5(6%)
Adenoid cystic carcinomas	2	-	-	-	-	-	1	3(3%)
Mucoepidermoid carcinomas	-	-	-	-	-	-	3	3(3%)
Melanomas	2	-	-	-	-	-	-	2(2%)
Undifferentiated carcinomas	-	-	-	1	-	1	-	2(2%)
Chordoma	-	1	-	-	-	-	-	1(1%)
Sarcomas	1	-	-	-	-	-	-	1(1%)
TOTAL	20	13	9	7	17	19	8	92(100%)

NPNS=Nose and Paranasal Sinuses, Npx=Nasopharynx, Opx=Oropharynx,
OC=Oral Cavity, Hpx=Hypopharynx, Lx=Larynx, Sg=Salivary gland (major).

The cancers of the nose and paranasal sinuses were more common accounting for 22% of the cancers of upper aerodigestive tract and the male: female ratio was 1:1 (table-

IV). The cancers of the nose and paranasal sinuses are more common as compared to the reports from other parts of the world, 3.6% from the Western literature and 13% from the Asian literature.[1,2,7] This higher incidence of these cancers in Kashmiri population could be because of the prevalent snuff use and exposure to wood dust and smoke of firewood used for cooking and heating purposes.

Tumors of oral cavity are rarer in this part of the world accounting for only 7.5% of the tumors of upper aerodigestive tract and male: female ratio being 1:1(table-IV) while as in western world it is the commonest site for the cancers of upper aerodigestive tract accounting for more than 30% of the cancers of upper aerodigestive tract and in most parts of India the incidence of oral cancers is as high as 50% of all cancers and oral cavity cancers are 3rd most common cancer in France.[1,2,6] This lower incidence of oral cavity cancers in Kashmir could be attributed to the absence of the habit of chewing of tobacco and alcohol intake in this part of the world and also to the lesser concentration of sticky foods like sweets and chocolate in average Kashmiri diet.

The cancers of the nasopharynx accounted for the 14% of the upper aerodigestive tract cancers and the male: female ratio was 1:1(table-IV) while as in Western world it accounts for only 3.4%and in other parts of Asia for 9%.[1,6] This could be taken as the indirect evidence of the possibility of viral oncogenic infections in the Kashmiri society besides other regional factors.

Table-IV: Upper Aerodigestive Tract Cancers: Frequency and percent Distribution and Male : Female Ratio of Each Site

SITE	No. Of Cases		%age	M : F Ratio (approx)
Nose & Paranasal Sinuses		20	22%	1 : 1
Nasopharynx		13	14%	1 : 1
Oropharynx (tonsils)		9	10%	2 : 1
Oral Cavity		7	7.5%	1 : 1.5
Tongue	3			
Palate	2			
Buccal mucosa	1			
Lips	1			
Hypopharynx		17	18%	2 : 1
Pyriform fossae	8			
Cricopharynx	9			
Larynx		18	19.5%	8 : 1
Supraglottis	6			
Glottis	12			
Salivary glands		8	9%	1 : 1.5
Submandibular	3			
TOTAL		92	100%	2 :

The cancers of the oropharynx accounted for 10% of the cancers of upper aerodigestive tract and the male : female ratio was 2:1.(table-IV) In western literature it accounts for only 8%of the cancers of upper aerodigestive tract and in other parts of Asia for 13%.[1,2,6] In all the 9-patients the site of origin were the faucial tonsils with Non-Hodgkin's Lymphoma accounting for about 50% of the lesions this is in contrast to the other studies were it contributes the 20-25% of the lesions.[7,8]

The cancers of the major salivary glands accounted for 9% of the cancers of upper aerodigestive tract and the male: female ratio being 1:1.5.(table-IV) In western population it accounts for only 5.6% and in other parts of Asian for 6% of the cancers of the upper aerodigestive tract.[1,2,9]

The cancers of larynx accounted for 19.5% of the cancers of upper aerodigestive tract while as in western countries it accounts for 28% and in other parts of the Asia it accounts for 26% of the cancers of upper aerodigestive tract. It is the commonest site involved in the cancers of upper aerodigestive tract in most parts of Asia and the second only to the cancers of oral cavity in Western population..[1,2,3,5,7] This is the only group of the upper aerodigestive tract cancers which is diagnosed in the early T1 / T2 stage because of the easily noticeable hoarseness of voice as the early presenting symptom and hence with overall better prognosis among all other cancers of the upper aerodigestive tract. The cancer is significantly commoner in males with approximate male: female ratio of 8: 1 (table-IV) this is in accordance with the reports from other parts of the world.[6]

The cancers of hypopharynx accounted for 18% of the cancers of upper aerodigestive tract and the male: female ratio was 2: 1. In western population it accounts for only 6.6%and also only 6.6% in other parts of Asia.[1,2,6] 60% of these lesions were arising from the cricopharynx and another 40% from the pyriform fossae. The higher incidence of these cancers in Kashmiri population goes in accordance with the overall higher prevalence of esophageal carcinomas in Kashmir which falls in the "Asian esophageal cancer belt" which extends from the northern province of China to the Caspian littoral of Iran.[10]

CONCLUSSION:

When compared with the results available from the western literature and from some parts of Asia the clinicopathologic profile was more like the Asian regions ,but still the individual regional variation could be appreciated in our study which speaks of the role of socioeconomic status, life styles, and other regional factors in the etiopathogenesis of these cancers, the absence of the use of oral tobacco and alcohol and the lesser incidence of cancers of oral cavity in this part of world could be used as the indirect evidence in the role of the former in the cancers of the oral cavity, and at the same time the higher incidence of the cancers of nose and paranasal sinuses, nasopharynx and hypopharynx in this part of the world stress the need of further studies needed in this direction.

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SURGICAL MANAGEMENT OF PILONIDAL DISEASE :OUR EXPERIENCE

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ABSTRACT: *There is no disagreement that the treatment of pilonidal disease is surgical with complete excision of the whole pilonidal sinus but controversy remains about what to do with wound after excision. Several techniques have been proposed. All of them try to reduce morbidity, offer fast healing, have a low recurrence rate and high cure rate. Minimal inpatient stay, minimal inconvenience and early return to work become important considerations.*

This study was under taken to evaluate the treatment of pilonidal sinus by excision and primary closure.

This study was under taken in Ohud hospital Medina Munawarah Kingdom of Saudi Arabia. The duration of study was three years and four months from May 2000 to August 2003.

All patients(82) treated during this period at Ohud Hospital Medina Munawarah with pilonidal disease were identified from the data base and details concerning their presentation, surgery and follow up were obtained from patient charts. All these patients were treated by excision and primary closure of the wound.

Eighty two patients, 75 males and 7 females were managed by excision and primary closure. The mean hospital stay was 5 days. Early complications like haematoma, wound infection, and minor wound breakdown occurred in 5% of patients. Two patients developed recurrence (2.3%). The mean follow up period was 6 months with a range of 3-40 months.

Excision and primary closure is a cost effective way of treatment for chronic pilonidal disease with low recurrence. Patient's compliance is very important. This treatment should be based on patient's preference and socio-environmental habitat.

Key words:*Excision, Pilonidal sinus.*

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INTRODUCTION:

Ever since the introduction of surgical treatment for pilonidal disease there have been modifications and reappraisals of various operative procedures from time to time that lead to the abandonment of some and improvement in others[1-5]. The quest for the ideal operation for pilonidal disease has not ended as none of the procedures offers complete freedom from side effects or low incidence of recurrence rates. The ideal operation for pilonidal sinus would be the one that is simple, free of mortality, low in recurrence and morbidity with shortened hospital stay. In the world literature there have been waves of enthusiasms in claiming better results for one operation over other. From Kingdom of Saudi Arabia very few reports[6] about pilonidal disease have been published even on internet Medline search. Present report evaluates our experience with 82 cases of excision and primary closure for pilonidal sinus.

Patients and Methods;

During the period from IstMay 2000 to 30th,August 2003, the data of 82 consecutive patients who underwent elective surgical treatment of pilonidal disease of the sacrococcygeal region at Surgical department of Ohud Hospital Medina, Kingdom of Saudi Arabia were collected into a computerized database using Microsoft Access programme. These patients were referred from government primary health centers, or other district hospitals and private general practioners. Acutely infected cases were excluded. All patients with chronic pilonidal disease were managed in the same way i.e. by excision and primary closure. After diagnosis, patients were prepared for surgical excision on outpatient basis. All these patients were admitted to surgical department of Ohud hospital for elective surgical treatment of pilonidal disease of natal cleft. Patients were admitted one day before scheduled surgery after history, clinical examination and investigations necessary for general anesthesia and for such type of surgery. Prior to shifting to operation room, patients were shaved from the gluteal skin crease to the mid-lumbar region extending laterally to the mid-axillary line. All patients received first generation

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Cephalosporin 1gm at the time of induction. General Anesthesia was given to all cases with endotracheal intubation. Patients were positioned prone, the buttocks were strapped apart, and the skin cleaned with povidone-iodine. Sinuses were probed to outline the tract. An elliptical incision with its lateral margins equidistant from the midline at a level that would allow apposition of the wound edges was made. The incision was carried vertically down with diathermy to the fascia overlying sacrum. Cutting with diathermy was done through grossly normal fatty tissue. All granulation tissue and hairs were removed. All tracts were opened, acutely angled skin edges were trimmed between tracts. Lateral tracts were excised by lateral extension of the incision without compromising the closure. To minimize skin gap, bridge of skin was kept intact. Bleeding was controlled with diathermy. Additional excision of laterally placed sinus with excision of the connecting tracts had to be done in some patients. One patient had multiple tracts like a flower. All excised specimens were sent for histopathological examination. Meticulous hemostasis was ensured. The wounds were irrigated with povidone-iodine solution. Full thickness deep tension sutures (using prolene 1) were placed at 1.5 cm from the wound margins at 2cm interval. After knotting surgically the long ends were left untied. The buttock straps were released .The fat was closed with interrupted 1/0 chromic catgut sutures in two to three layers according to thickness of the fatty layer. Some of the deep sutures were taken to include the sacrococcygeal fascia. Vacuum suction (Redivac) was done over sacro-coccygeal fascia in patients with multiple sinus tracts or obese patients with deep seated lateral tracts in order to avoid post operative collection or haematoma. The drain was removed when there was no discharge usually after 24 –48 hours. The skin edges were closed with interrupted 2/0 sutures polypropylene (Prolene, Ethicon Inc. Somerville. NJ) at the same time taking care to have accurate apposition of edges. Before closure one gram of Cephalosporin incorporated in twenty ml of normal saline wash was given locally to the wound. The skin was cleaned with saline and betadine soaked roll gauze was placed over the length of wound. Deep tension sutures of 0 polypropylene (Prolene, Ethicon Inc. Somerville, NJ) whose long ends were left untied were tightened over the roll gauze soaked in betadine (povidone iodine solution). Strap tight dressing was applied for forty eight hours. Post operatively patients were given liberal analgesia. Patients were advised to sleep prone and demonstrations were given as to how to get out of bed without putting much tension on the suture line. Light laxatives were given to avoid constipation and unnecessary strain. In early period of this series we used to discharge patients on second post operative day. This policy of early discharge had to be revised keeping in view socio environmental conditions of patient. Patients were kept in hospital till fifth day when tension sutures would be removed. All the discharged patients would receive five days course of oral Cephalosporin one gram eight hourly and Metronidazole half gram eight hourly. Instructions were given at the time of discharge to keep their natal cleft bereft of hair either by shaving or by using depilatory creams. All patients were advised to have bed rest for two-weeks with instructions for avoiding prolonged driving especially in hot climates for six months periods. Patients were instructed to avoid prolonged driving, lifting heavy weights, playing football (usual past-time for local youths) at least for three months time. Follow up was conducted in post operative clinics on ninth day when the sutures would be removed. Patients were reminded regarding removing hair at natal cleft and measures to avoid tension on natal wound. Patients were advised to have follow up examination at three weeks interval in out- patient clinic until the wounds were completely healed. During these times assessment regarding shaving hair at the backs and natal region was done and advised. Further follow up was conducted at three months and then at six months for a mean period of 12-24 months. After two years patients were advised to return to our clinic in case of any discharge or bleeding from the operation site. During this period any complication was recorded. Patients were advised to return if they developed any problem related to their pilonidal disease. For long term follow up patients were instructed to contact the hospital for any assistance.

RESULTS.

The results are summarized in Table 1.

Table 1: Summary of results of excision of pilonidal sinus with primary closure.

Total number	82
Male : Female	10:1
Mean age	27.5 (17-38) years
Average inpatient stay	5 days (3-11days)
Early complications	4 (5.0%)
Average follow up period(range)	23.5 (3-40 months)
Recurrence rate	2 (2.3%)

There were 82 patients between age ranges of 17-38 years. 75(91%) were males and 7 (9%) were females. The average inpatient stay was five days. Two patients had prolonged stay in hospital up to ten days. Out of these one patient had to walk long distance to reach home. Another patient was amputee who had lost his leg in an accident and his sinuses were situated just above anal verge. This patient was a potential case who could secondarily be infected we had to keep him in hospital for long time till his sutures were removed. Seventy four patients (90%) achieved complete wound healing with no evidence of infection at the time of suture removal. When assessing the early complications, four (5%) patients had wound break down, two because of wound infection and two because of serum collected in the wound. These patients had superficial dehiscence and were treated conservatively. With repeated dressings complete healing was achieved within six weeks Two patients (2.43%) developed recurrent pilonidal sinuses at one and three months post operatively. One of them had multiple sinuses with diabetes and the other one had poor personal hygiene The average period of follow up was 23.5 months (3-40 months).

DISCUSSION:

Pilonidal disease and its management has remained the subject of enormous clinical and scientific debate for many decades as evolving treatments for diseases of unknown etiology invariably become topics of controversy and contentious wrangling. Since Mayo reported first case of pilonidal disease in 1833[7] many methods of treatment ranging from simple injection of phenol or hair removal to extensive plastic constructions have been advocated. But no procedure has been free from criticism. There is no disagreement that the treatment of pilonidal disease is surgical with complete excision of the whole pilonidal sinus (8,9) but controversy remains about what to do with the wound after excision: should it be closed primarily[10,11,12] or be left open[13,14,15] or closed by fascio-cutaneous and musculocutaneous flaps[16-19] or have the edges marsupialized[20]. With wide range of operations ranging from flaps to open method, the failure rate of treatment with most of procedures is still high. In fact there is no single operative procedure for pilonidal disease, which has been universally accepted. The ideal surgical treatment of pilonidal disease still remains unresolved. Each method of treatment has its advocates judged by the yardsticks of primary healing and recurrence of disease. An ideal operation should be simple, should have a shorter hospital stay, have a low recurrence rate, and be associated with minimal pain, and cost effective and wound care to decrease the off work time[1].

Simple shaving and removal of hair may control symptoms without operation[21]. Surgery is often required when chronic infection supervenes. Brushing of pits, then a novel method, advocated by Lord may be used in minor disease with healing time of 21-52 days with recurrence rate of 3-24%. Application of phenol to the pits has been used with 0-35%recurrence rate, healing time of 14-61 days[22-25]. Complete excision of the pilonidal sinuses with excision of secondary tracts down to the sacral periosteum is essential to minimize recurence. The resulting deep wound should be left open to granulate because primary closure may result in excessive skin tension and subsequent dehiscence. Until the beginning of World War II radical excision with wound healing by open granulations was used. Excision and open packing is known to have a low recurrence rate of 4-6% however it requires multiple dressings and may take weeks to heal (median 3 months)with considerable loss of working time[26-28]. To hasten the wound healing process alternative techniques like use of extensive flaps were used. with low recurrence rate of 4-6%[1,29] but it takes31-90 days to heal ,median 3months[30] with considerable loss of working time[13,18,31,32].

The ideals for any procedure that the procedure has to be simple, early return to work, minimal hospital stay, and low recurrence rate are goals of treatment. Lee et al[33] in his study of outcome of various operative procedures done for pilonidal disease showed no advantage of the complex flap procedure over the simple techniques which requires lesser operative time and shorter hospitalization care.

As the method of excision and primary suture was introduced it faced criticism due to difficulties of the closure and so called "death space" developing after extensive excision[34]. Frequent failures reported that time with primary suture to close dead space lead to the use of numerous other methods with free or rotation flaps or musculofascial flaps[35].Some of them are major plastic reconstruction procedures to be done for this disease[36-41] None of the suggested methods is free from recurrence[33] or inherent problems like multiple painful dressings and prolonged healing time. Excision with primary closure provides quicker healing and return to work in three to four weeks[11,17,42]. The rates of wound breakdown and recurrence however have varied significantly among various reports 20-50%[9,43-45]. We report our series of consecutive 84 patients undergoing excision and primary closure.

The principles behind the operative technique have been described by many[26,40]. The aim of primary closure is rapid healing .This can be achieved by the prevention of sepsis and haematoma formation which is the common cause of early wound breakdown[42].To decrease the incidence of wound breakdown, primary closure is done in a way that includes deep tension sutures. Additionally using vacuum suction drains has been effective in preventing these complications[11].

Deep tension sutures and drains only add to pain ,discomfort and prolong stay in hospital without having any obvious advantage regarding the outcome benefit[30]. didn't hold true for our patients. Further deep tension sutures not only fails to prevent haematoma but encourages infection by prolonged contact with the pack , which traps wound exudates and spreads bacteria down the suture tracks was reported by Willams et al[42]. He reported that simple primary closure without tension sutures but with drains resulted in primary healing in 28 of 31patients. However hospital stay in this group of patients was slightly prolonged to four days because of the presence of drains.

On the other hand when suction drains were omitted but tension sutures were used together with a prolonged course of antibiotics Khaira et al[11] could reduce hospital stay to one day with an early complication rate of 9% and a debatable recurrence rate of 18%. By adopting the simple closure technique and omitting both tension sutures and drains Jaberi[30] claimed that he could reduce hospital stay of patients to 48 hours. The wound disruption rate of 7% and recurrence rate 4% after a mean follow up of period of 36 months in the study of Jaberi[30] is comparable to the results using drains and tension sutures[11].

The criticism that drains and tension sutures add only discomfort to patient and prolong the stay in hospital until the drain is removed which may be true[4]. But each patient has to be treated according to his or her merits to avoid post operative complications. When the risks and benefits are explained to the patient we found that tension sutures were well acceptable to our patients without any additional inconvenience.

For the question of using a drain or not to drain wound Al-Jaberi[30] recommends drain only in selected patients. His earlier practice of using drains in all patients did not show any benefit thus it did not justify its use. We used selectively redivac vacuum suction drain in patients .Patients with poor compliance or who had deep rooted sepsis or multiple tracts. the vacuum suction drain was put for 48-72 hours .This selective policy of using drain in particular type of patients has helped us in decreasing the incidence of early complications in this high risk group. To minimize wound dehiscence or infection meticulous attention has to be given to hemostasis and the use of "fat stitch" tight closure of the fatty layer to decrease subcutaneous cavity. This not only prevents early complications of hematoma formation but allows early discharge of patients from hospital[11]. Early complication rate of 5.0% in our study are slightly better but comparable with 8.6 % and 6.4% as has been reported by Khaira and Williams in their studies respectively[11,42].

All our working patients were back to work within two to three weeks period similar to Jaberi[30] with selective use of tension sutures and drains. To achieve good results patient compliance and cooperation is necessary. The personal hygiene, habits, social environment, customs, body weight and types of employment of the patients all have to be taken into consideration .We used to discharge patients earlier in the beginning of this study but wound disruption rate was found high (3.57 %, 3/84). Probing deep into socioeconomic environment and habitat of patients we found that patient compliance in this respect was poor and some of these patients didn't strictly comply with our post operative instructions .They either lived alone and had to do their domestic work themselves or they would not restrain themselves from driving with incompletely healed wounds. By not taking home rest they were more susceptible to wound dehiscence. We preferred to keep our patients in hospital till fourth day when we removed drain or tension sutures and as per wound situation then patients would be discharged to home. It was stressed on all patients that to follow strictly instructions like avoiding driving in hot climate and wavy roads, not to lift heavy weight, treating constipation early and keeping natal clefts bereft of hair are important for preventing recurrence. These all alone or in combination has worked 1 in decreasing wound disruption and recurrence rate in our present series.

The ideal treatment should involve minimum inconvenience and time off the work. Initial time to healing in our series was 12days ,which is almost same as reported by Khaira et al[11]. This is considerably less than the time taken to heal when patients were treated for excision alone with average period of 3 months[1,13,15]. Majority of our working class patients returned to work in 3-4 weeks, again similar observation like previous reports[11,42] This compares with 42 days reported for excision only[31]. Bacteriological examination of pilonidal sinuses have shown the presence of staphylococcus and bacteriodes species in at least 50% of cases[13,46] thereby increasing chance of infection and dehiscence. We adopted a policy of short course of antibiotics that covers both staphylococci and bacteriodes species. This was based on reports that the use of antibiotics decreases the time to healing after primary closure[47]. We agree with Jaberi et al[30] that using a longer course of antibiotics contradicts our basic assumption that such wounds are clean enough to be closed primarily.

The pilonidal disease does not impose diagnostic difficulties, however, it causes a considerable therapeutic problem and high recurrence rate. The disease has wide recurrence rates ranging from 3.3% after extensive plastic reconstructive methods to 38% after the method of excision and primary suture[11,48,49].

The failure of the treatment for pilonidal disease of the sacrococcygeal region was until recently thought to be related to surgical and technical difficulties of wound closure in the intergluteal region. That is why we have number of modifications for closure of the surgical wound of the intergluteal region[34,50]. Lately, greater emphasis has been given to the importance of bacteriological characteristics of the pilonidal disease of the sacrococcygeal region. Literature reports point to high rates of the bacterial colonization in the pilonidal sinus, found in 88.5% of patients admitted for surgical treatment. Anaerobes predominate in the bacteriological tests, both in mixed and pure cultures. The anaerobe versus aerobe rate is reported to be 5 to 1[50-55]. When planning a surgical treatment and applying particular surgical method one has to take into account the high bacterial colonization in the pilonidal sinus[34].

In our series late recurrence rate at a mean follow up of 23.5 months was 2.3%.this is comparable to and in some cases better than previously published series of primary closure[1,4,13,15,20] this compares with recurrence rate of 0-43% for laying open of pilonidal sinus down to sacral fascia[1]. Our follow up period is relatively short and early recurrence is believed to be due to persistence of tracts lined with granulation tissue in an incompletely healed wound[56]. However specimens from all our patients were subjected to histopathological examination. It showed complete excision in all cases even in patients who had disruption and recurrence. This patient admitted that he went for prolonged driving with unhealed wound in hot summer and rough desert roads. Notras[26] states that hair is found in late recurrences. Hair was seen in only in one of the three cases in our series who had recurrence dealt with. We can therefore safely assume that the recurrences to be true recurrences rather than failure of initial wound healing. The distinction between delayed healing and true recurrence needs to be considered. The latter represents incomplete excision of the pilonidal sinus at its initial surgery or the formation of a new pilonidal pit and sinus. Delayed healing may also result in a track of granulation tissue with hair. As mentioned above the presence or absence of hair has been used to indicate true recurrence; however some prefer to define true recurrence as occurring more than 12 months after surgery[1,20]

We therefore advocate that this method of treating pilonidal disease by excision and primary suture , which has minimal hospital stay, minimal morbidity, short time off work, and lesser recurrence.

CONCLUSION ;

Pilonidal disease is a benign condition and patients apparently outgrow its infective complications. It is therefore. imperative that the treatment is no worse than the disease itself. Prolonged time away from work and unhealed wounds are avoidable, treatment can now be offered as a day care without admission to over committed hospitals. When wounds do not heal simple surgical techniques exist that can overcome the problem. Excision and simple primary closure of pilonidal sinus carries the advantages of quick healing and low rate of breakdown and recurrence. Although deep tension sutures and drains add to discomfort, and prolong stay in hospital but they offer advantage in terms of recurrence. Flaps and extensive plastic operations are to be reserved for recurrent and complicated cases[57,58,59].

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MANAGEMENT OF DUODENAL PERFORATION IN A RURAL HOSPITAL

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Abstract: *4 patients operated for duodenal perforation are presented. Features of peritonism were present in 2, peritonitis in 2. All were closed by an omental patch, 3 patients are doing well at a follow up of 3-5 years.*

Key words:- *Duodenal perforation, Spinal anaesthesia, Omental patch closure.*

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Introduction:

Acid peptic disease is among the most common ailments in this part of country. One of the complications of peptic ulcer is duodenal perforation. The incidence of perforated peptic ulcer is approximately 7 to 10 per 1 lac population per year[1]. In about 2 percent of patients with duodenal ulcer, perforation is the first manifestation of the disease. After the diagnosis of duodenal ulcer 0.3 percent of the patients perforate in the first 10 years. The risk factors for perforation include non steroidal anti-inflammatory agents, immunosuppression, steroids, elderly patients, chronic obstructive lung disease, major burns and multiple organ failure[2-5].

Quick diagnosis and immediate surgical intervention gives excellent long term results. Closure by an omental patch is considered to be the best.

Materials and Methods:

The study was conducted in a rural hospital over a period of more than 3 years. A detailed history thorough general and systemic examination was contemplated. Plain skiagram abdomen and chest was done. Haemogram and blood grouping was done in all, besides serum urea, serum creatinine and blood sugar was also done in 2 patients. Immediately after suspicion/diagnosis patients were put on intravenous line, nasogastric suction, antibiotics, H_2 blockers or proton pump inhibitors and nothing was given orally. All 4 patients who refused referral or could not be referred because of one or the other reason were operated. Spinal anaesthesia was given in all and sensocaine was the drug used. Duodenal perforation closure was performed by Omentopexy. Intraoperative problems post operative complications were recorded in all. Oral sips were started after 3rd through 5th postoperative day. Patients were discharged after 9th post-operative day.

Evacuation, suction, mopping of all the gastric contents, peritoneal fluid and purulent material was done. Thorough peritoneal lavage was done in all. In two patients with delayed presentation/trimming of the friable edges was done before closure.

Observation:

The patients were in 3rd through 6th decade of life and all were males, 2 were labourers, one a driver and one 57 years old, a farmer by profession. 3 patients were smokers and alcoholics. 2 patients presented with classical symptomatology of duodenal perforation though the surgery was delayed by 10-12 hours. Late presentation was observed in 2 patients one of them had carcinoma stomach. Pain abdomen vomiting was present in all. One patient had associated constipation. History of alcohol consumption in 2 and analgesics intake was present in 1. One had associated anaemia, anorexia, Paller in 1, tachycardia in 4, scattered bilateral crepts chest in 2, obliteration of liver dullness in 3, board like rigidity in 2, features of ileus in 4, tenderness abdomen in 4, tender per rectal examination in 2 and pyrexia in 2 patients were the clinical signs observed.

X-ray evidence of gas under the dome of diaphragm on right side was observed in 3 patients. One patient was anaemic Hb <8gm/dl. Spinal anaesthesia was used in all. The operative findings were, duodenal perforation in 4 patients food contents in peritoneal cavity 3, right iliac and pelvic purulent collection in 2, lesser curve mass with celiac nodes in 1, and fibrous band over ileococal region in 1 patient.

Closure of the perforation was performed by omentopexy (fig. 1). In addition, biopsy from gastric mass and celiac nodes in 1 and release of band was done in one patient. Corrugated rubber drain was kept in all. The surgery lasted from 2 to 4 hours. Ryles tube was removed after 3rd day when bowel sounds were present. Oral sips were started after 3rd day and by 5th day patients were on liquid diet. Drain was removed after patients were on

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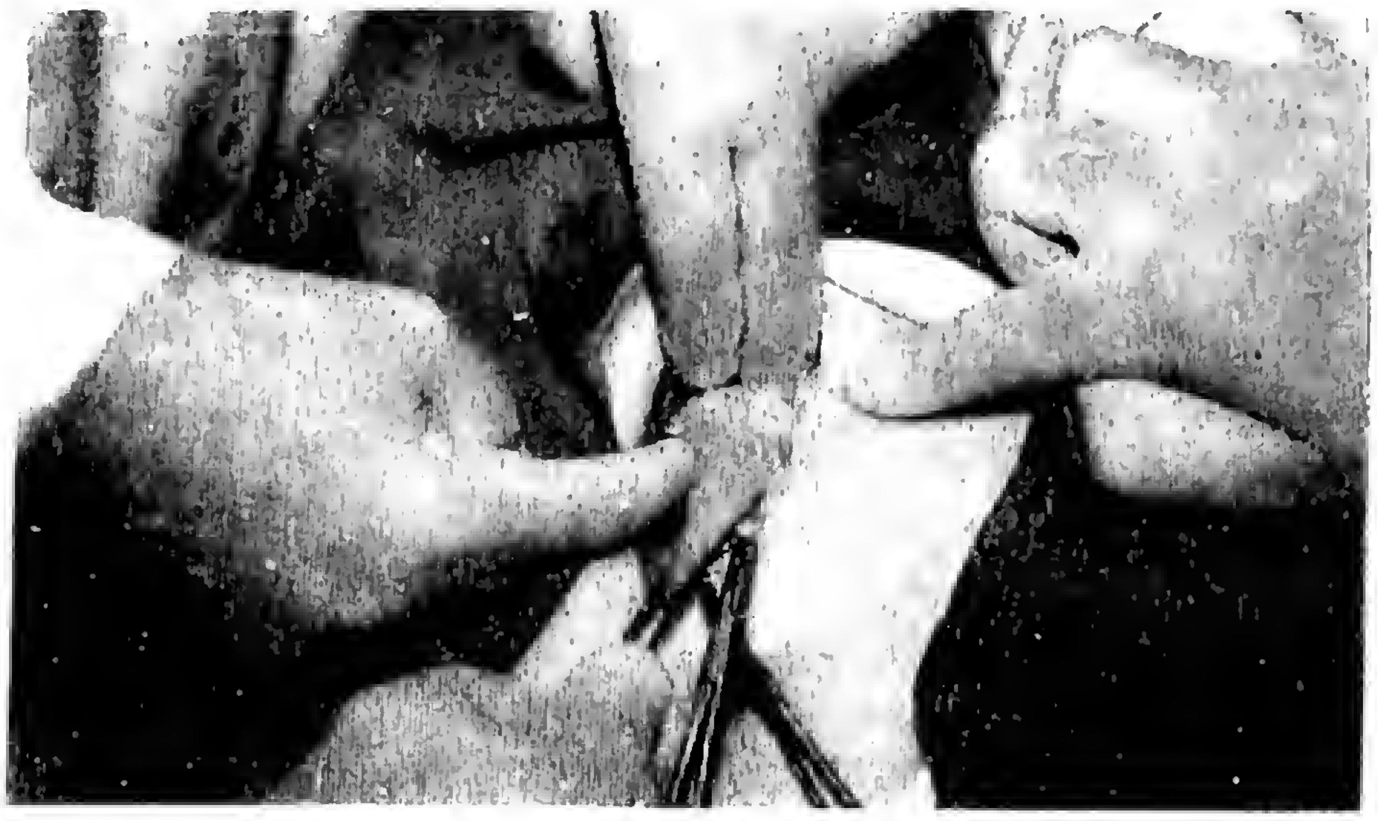

Fig.1: Contents Seen Coming out of Duodenal perforation

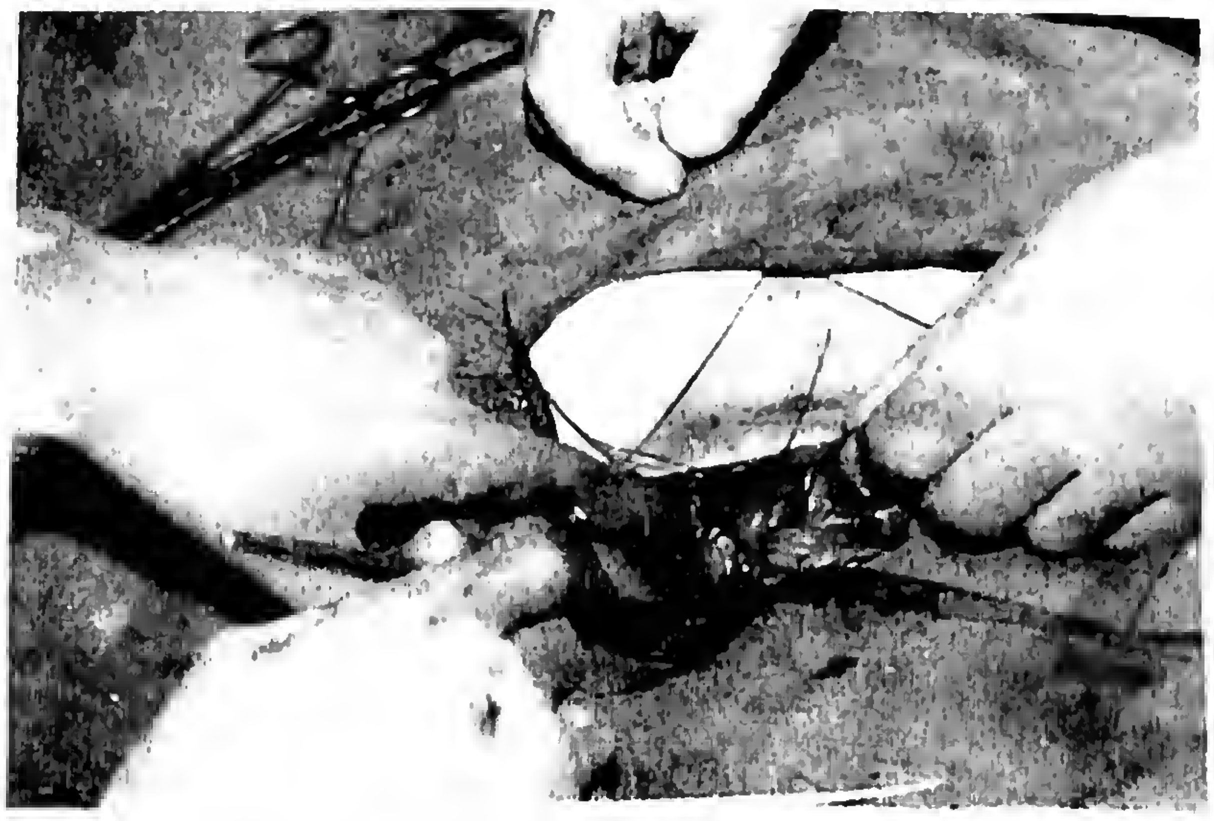

Fig.2: Closure of the perforation using omental patch.

full semisolids and had no clinical evidence of leak or peritonitis. All patients were discharged alive. However, one who had carcinoma stomach died 2 months after surgery. Three patients are doing well at a follow up of 3 to more than 4 years.

Comments:

Though a very small number of patients it is pertinent to mention even about this meagre number, because it has been conducted in a rural set up where all the facilities of tertiary care centre are not available. Symptoms and signs of acute abdomen are present initially followed by generalized peritonitis, liver dullness to percussion may be replaced by tympony[6]. Chest PA, supine and left decubitus abdominal skiagrams are generally obtained[7]. However, investigations should not delay the surgical intervention. Ideally these patients should be operated within the hour of presentation, intervention after 24 hours increases morbidity, mortality and hospital stay[8]. After ulcer closure a definitive acid-reductive procedure is performed and proximal gastric vagotomy is performed whether or not the ulcer is chronic[9-12]. In none of our patients was such a procedure performed because all had almost delayed surgery and gross abdominal contamination with food and purulent material was present.

Of late the other causes of duodenal perforation are laproscopic cholecystectomy, endoscopic sphincterotomy and enteric fever[13-14]. Accordingly the closure can be done by omental implantation, omental patch, falciporm ligament, jejunal serosal patch technique, pyloroplasty, duodenostomy and resection.

In summary, duodenal perforation is very common in this part of country, can present with a grim phenomenon because of profound derangement of 'milieuinternals' especially in delayed presentations elderly patients, or in patients with concomitant medical problems.

In conclusion omental implantation is a simple, dependable and preferred choice, and can be performed easily even in a community health centre.

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OPEN REDUCTION AND INTERNAL FIXATION OF FRACTURES OF SURGICAL NECK HUMERUS.

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ABSTRACT: *Open reduction and internal fixation was employed in the treatment of 10 fractures of the surgical neck of humerus in whom closed reduction had failed. Our aim was accurate reduction and stable fixation to allow early rehabilitation and to achieve full functional recovery. In all cases an AO "T" plate was used for fixation of these fractures. Excellent or satisfactory results were obtained in nine of the patients, and one of the patients had an unsatisfactory result, due to periarthritis which he developed in the post operative period.*

Key Words: *proximal humerus fractures, open reduction and internal fixation, AO technique.*

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Fractures of proximal humerus are challenging to diagnose and treat. Much information has been published in recent decades about these injuries, as new techniques of treatment have been developed and old ones are rediscovered.Hippocrates[1], is credited with documenting the first proximal humerus fracture in 460BC,and describing a method of weight traction that aided in bone healing. However little was written about this subject until the latter part of the 19th century[2,3,4, and 5]. In 1896,Kocher[6], developed an anatomic classification in an attempt to improve diagnosis and treatment. In 1934,Codman[7], made a significant contribution when he divided proximal humerus fractures into four basic parts. Neer[8,9] ,in 1970,proposed four part classification based on the anatomic classification.It is a comprehensive system that integrates fracture anatomy, biomechanics and displacement. It remains the most useful and common classification system for proximal humerus fractures. In the early 20th century, methods of closed reduction [10], traction [11], casting[12],and abduction splints[13], were developed to achieve and maintain accurate anatomic alignment of displaced fractures. Often these closed techniques were not sufficient to allow an adequate anatomic reduction. Howard and Eloesser[14],developed a complex theoretical shoulder model simulating muscle forces and demonstrated that the abduction splint was not beneficial for reduction and control of muscle forces. Open reduction of severly displaced fractures gained popularity during the same period in an effort to provide better anatomic alignment [15,16,17,18]. Robert[19], and Meyerding[20], suggested the use of open reduction at an early stage to improve alignment and avoid malunions that would limit motion. In 1949, Wisden[21], first reported on intramedullary nailing of these fractures. In the early 1970's the association for the study of internal fixation group popularized the use of Ao plates and screws for displaced fractures[22]. In 1983,Paavolainen et al[23], reported use of "T" plates for these fractures with overall satisfactory results. In 1990,Moda SK,et al,[25],reported their results on use of T plates for proximal humerus fractures with overall good results.

For full functional recovery anatomic reduction, stable fixation and early mobilization are required. With these requirements in mind, we treated Surgical neck fractures of humerus with AO 'T' plate.

Materials and Methods:

From Jan 2002 to Feb 2003 we treated 10 cases of surgical neck humerus fractures at Govt.hospital for bone and joint surgery,Srinagar by open reduction and internal fixation with AO 'T' plate. All were two part surgical neck humerus fractures based on Neer's classification. These cases selected for this study had failed closed reduction

Technique of operation:

With the patient under general anesthesia and in supine position, the fracture was exposed using delto pectoral approach taking care not to dissect the soft tissues beyond the medial border of the lateral lip of bicipital groove. The fracture fragments were reduced under direct vision and fixed with AO 'T' plate. In all the cases the plate was applied lateral to the tendon of the long head of biceps[26], and special care was taken to ensure that the upper end of the plate did not impinge on the acromion when the arm was abducted. AO 6.5mm cancellous screws were used in the cancellous bone proximally taking care not to

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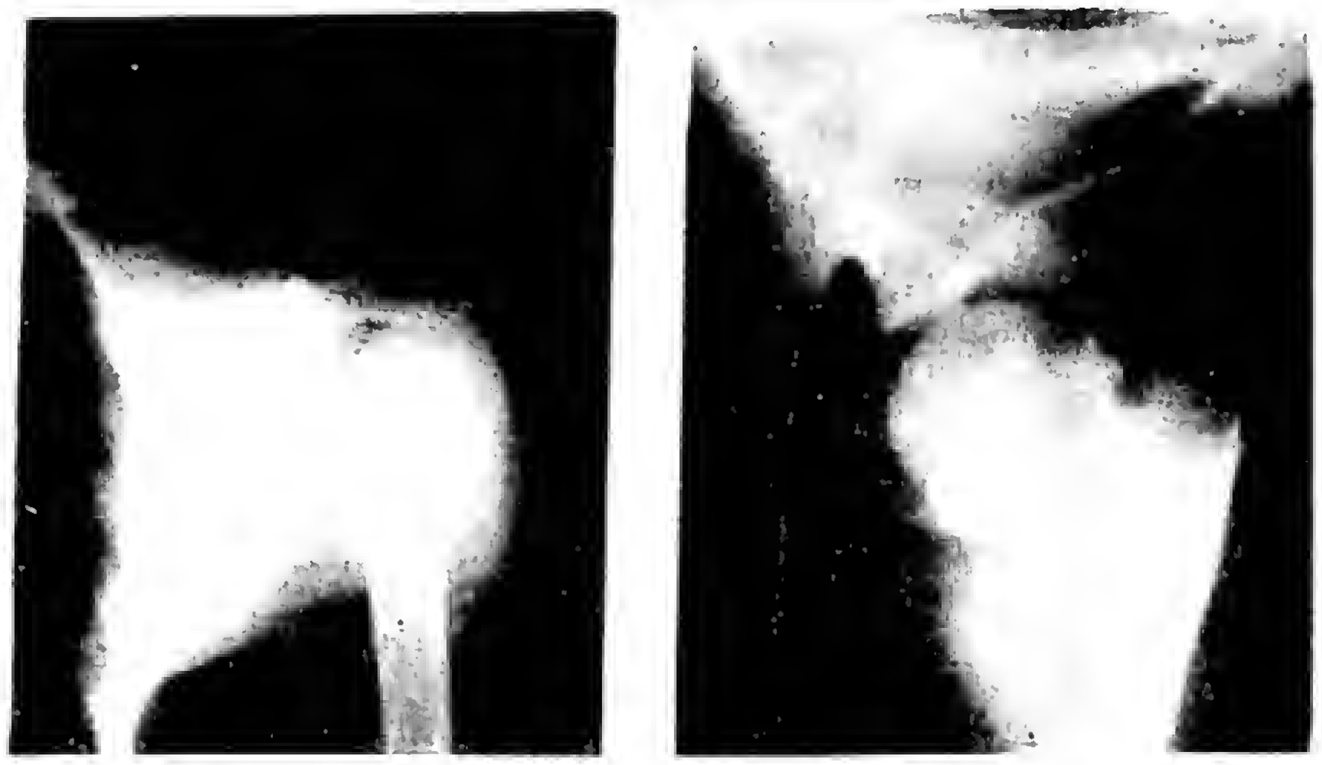


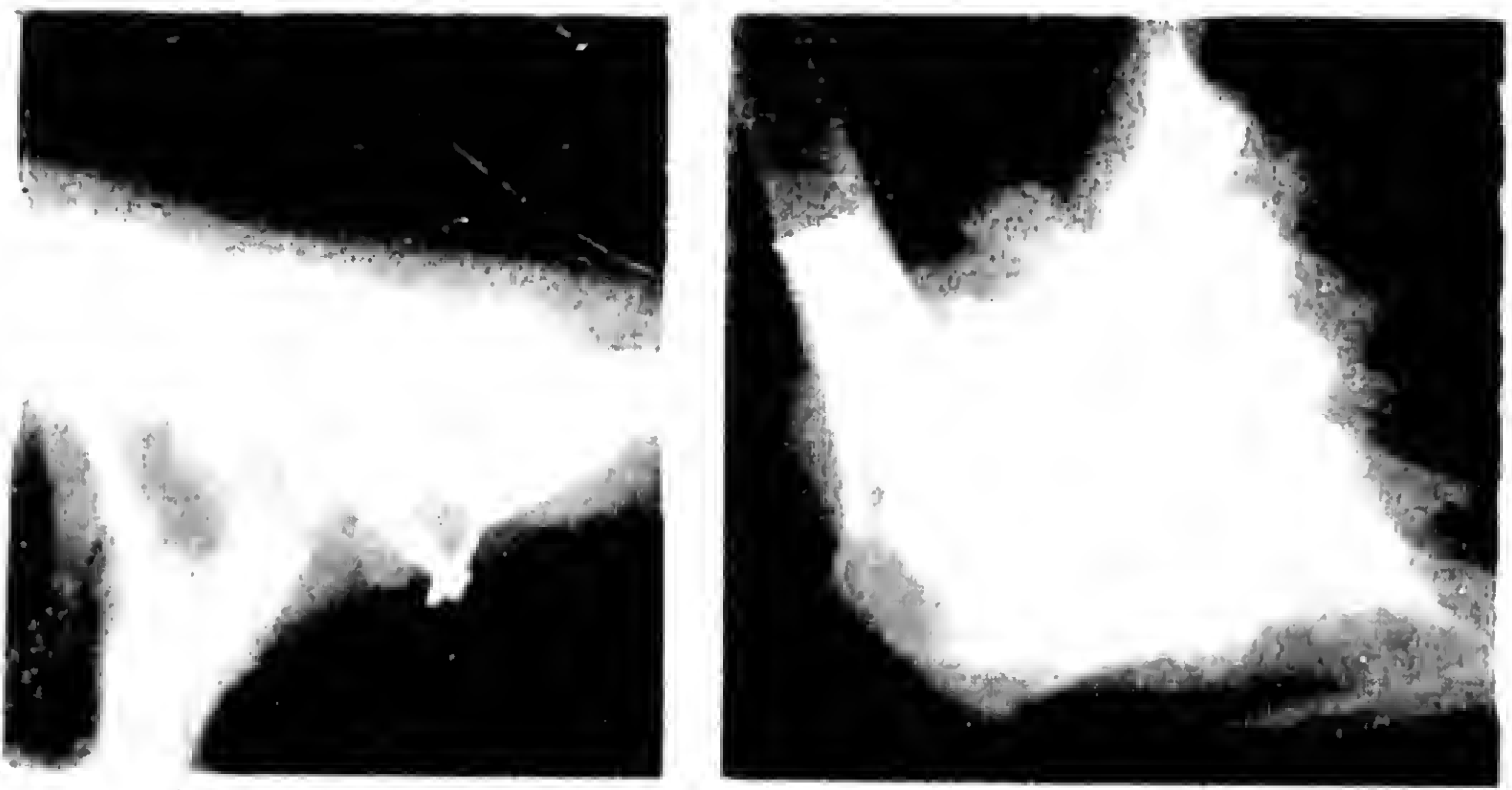
(AP veiw) *(Axillary view)*

Pre-Operative roentgenograms (Fracture Surgical Neckof Femur)

penetrate the joint, and 4.5mm cortical screws were used for the fixation of the distal fragment. The wound was closed over a suction drain and post operatively the arm was wrapped in a sling and swath. Rehabilitation of the shoulder was started 24-48 hours later based on the three phase rehabilitation protocol devised by Hughes and Neer[24].

Observations and results:

Ther were 7 men(70%) and 3 women(30%) aged 23-48 years(avg.30.4 years). The commonest cause of injury was a road traffic accident(60%) and fall on an outstretched hand in (40%). The right arm was involved in 7 of the patients and left arm in 3 patients. An AO 'T' plate was used in all the 10 patients. Results were evaluated using the score system of Neer [8,9],which employs a maximum of 100 units distributed as following: Pain 35, Function 30, range of motion 25, Anatomy 10. An excellent score is 90 or more, satisfactory 80-89, unsatisfactory 70-79, and a failure scores less than 70 units. Analysis of our results is shown in Table 1.



(AP veiw) *(Axillary view)*

Pre-Operative roentgenograms (Fixed with AO "T" Plate and Screws)

No.of cases.	*Neers criteria.*		
	Excellent.	*Satisfactory.*	*Unsatisfactory.*
10.	3.	6.	1.

Unsatisfactory result in one of our patients was attributable to non compliance with the rhabilitation programme resulting in periarthritis of the shoulder. We had no major complications such as osteomyelitis, avascular necrosis, non-union or implant failure. Technical problems like high positioning of the plate, unstable fixation or screw penetration of the joint were avoided.

Discussion:

The major disadvantage of closed methods in the treatment of displaced fractures of the proximal humerus have been reported to be poor reduction, instability leading to secondary displacement and prolonged rehabilitation time [27,28]. Open reduction and internal fixation offers satisfactory stability, but it is a demanding technique, sometimes leading to technical error,with a risk of damage to the remaining blood supply to the head of humerus and avascular necrosis [22,23]. The shoulder is especially susceptible to stiffness following injury because of formation of adhesions. Early mobilization prior to maturation of adhesions around the joints gliding surfaces is therefore, an essential step in the management of proximal humerus fractures. The AO 'T' plate, properly applied achieves fixation stable enough to allow immediate mobilization. In our study we achieved excellent or satisfactory results in 90%, an improvement over some of the previously reported series. Paavolainen[23], in 1983 reviewed 41 cases of which 74.2% were excellent or satisfactory. Moda et al[25], in 1990 reported excellent or satisfactory results in 84%.

We attribute the successful results in part to the avoidance of technical errors like limiting the soft tissue dissection,high positioning of plate, an unstable osteosynthesis and penetration of joint by screws. We think it is important to use 6.5mm cancellous screws for fixation in the epiphyseal area. In our series no patient had nonunion or avascular necrosis nor have these complications been reported by others [22,23,25]. The rigour of the rehabilitation protocol had a significant bearing on the range of motion achieved and the overall functional recovery of the shoulder joint.

Conclusion:

We conclude that two part fractures of the surgical neck of humerus treated by early open reduction and stable fixation with an AO 'T' plate with adherence to the adequate technicalities and an early start to fixation with an AO 'T' plate with adherence to the adequate technicalities and an early start to physiotherapy heal with overall satisfactory functional recovery, with very few complications.

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METACARPAL LENGTHENING BY DISTRACTION OSTEOGENESIS

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Abstract: *Distraction osteogenesis using UMEX distracter was used in five patients with brachymetacarpia between 1999 and 2002. All of the patients were females in an age group of 15-20 years (mean 17 years). All the patients achieved desired length and aesthetic improvement of hand. Average length achieved was 23 mm and an average healing index was 1.3 months /cm. Except for mild pain and minor pin tract infection there were no major complications. Distraction osteogenesis can be used safely in the treatment of isolated brachymetacarpia.*

Key Words: *Brachymetacarpia Distraction Osteogenesis, Callotasis*

JK-Practitioner 2004;11(1):32-34

Introduction:

After the success of distraction osteogenesis in limb lengthening, the technique is finding new applications in the management of congenital and acquired hand deficiencies. Procedures' involving staged reconstruction of digits and thumb in addition to being painful have a high rate of complication and require multiple surgical interventions[1]. The ability of distraction osteogenesis to reconstruct with the limited tissues available in the deficient hand provides an alternative reconstruction procedure with predictable results. In order to improve the function of hand, the accepted indications of distraction osteogenesis are patients with absence of multiple digits, hypoplastic thumb with some functional thenar musculature, loss of intercalary bone stock and amputations with transverse terminal arrest to improve prosthetic wear[2]. The availability of small miniature external fixators has made lengthening procedures in small bones of hand easy and the fixation stable. In this paper we review the use of this technique in the treatment of isolated brachymetacarpia.

Material and methods:

We reviewed the results of metacarpal lengthening in five patients operated between . 1999 and 2002 at the hospital for bone and joint surgery Srinagar. All the patients were females in an age group of 15 to 20 years (mean 17 years). The complaint at presentation was pain at the metacarpophalyngeal joint and all of them were concerned about the appearance of their hand. Patients were operated upon using distraction osteogenesis. In four patients UMEX distracter was used and in one patient a locally made distracter was used.

Surgery was performed under general anesthesia and under tourniquet controt. In view of the mini external fixator to be mounted on the metacarpal we preferred to perform the osteotomy of the metacarpal before applying the apparatus. The metacarpal was apptoached through a dorsal one cm incision. After retracting the extensor tendon to one side, osteotomy of the metacarpal was performed aiming towards the metaphyseal end of the bone. The proximal and the distal fragments were then fixed with two threaded wires (1.5mm) one in each & fragment on either side of the extensor tendon making sure not to fix the tendon. Two pins were used in each fragment in one patient in whom a locally made distracter was used. The mini apparatus was then mounted and skin closed with silk and tourniquet released. Patient received prophylactic antibiotics for three days. Post operatively the hand was elevated and analgesics administered as and when required. Patients were discharged from the hospital on first postoperative day. Distraction was started after a gap of seven days and at the rate of 0.25 mm thrice daily. Patietns were followed every week initially till the length was equalized and then every three weeks till consolidation of the regenerate. Special attention was paid to know the distraction, pin site care and function of the hand. The rate of distraction was adjusted according to the appearance of regenerate on X – Ray. During the whole process of lengthening and consolidation the patients were encouraged to do physiotherapy. The apparatus was removed when the gap was found to be bridged by the solid new bone.

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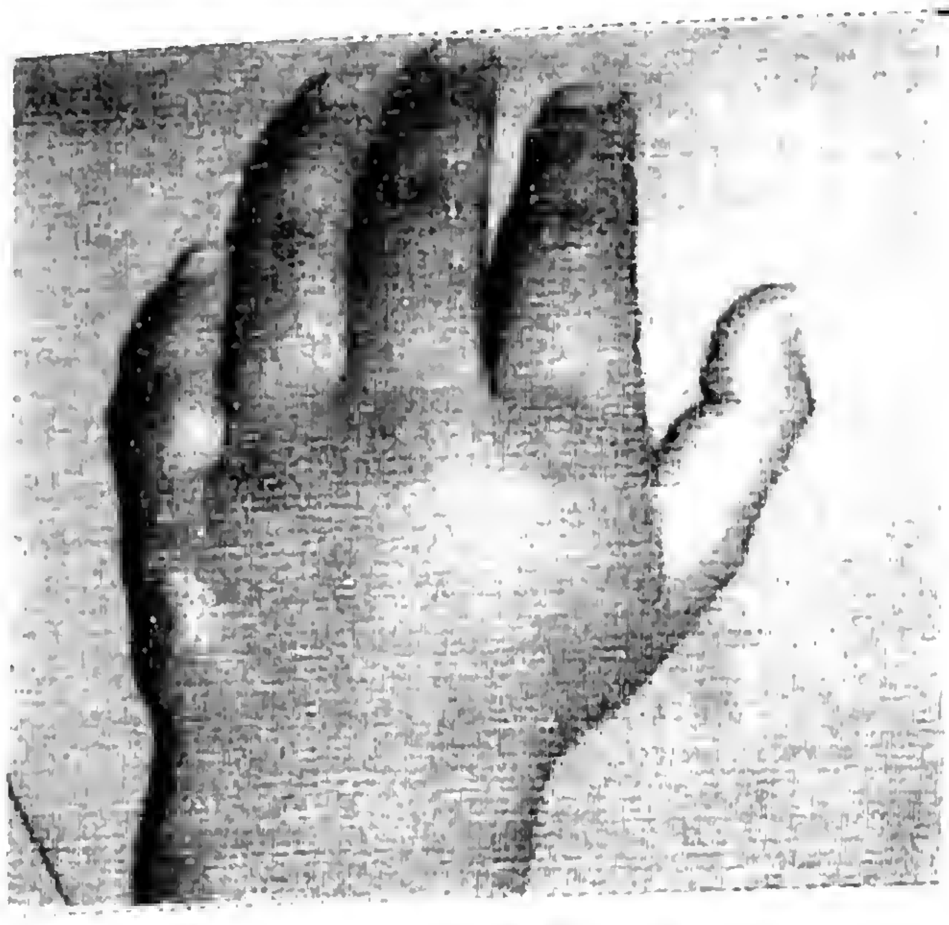

Fig. 1a

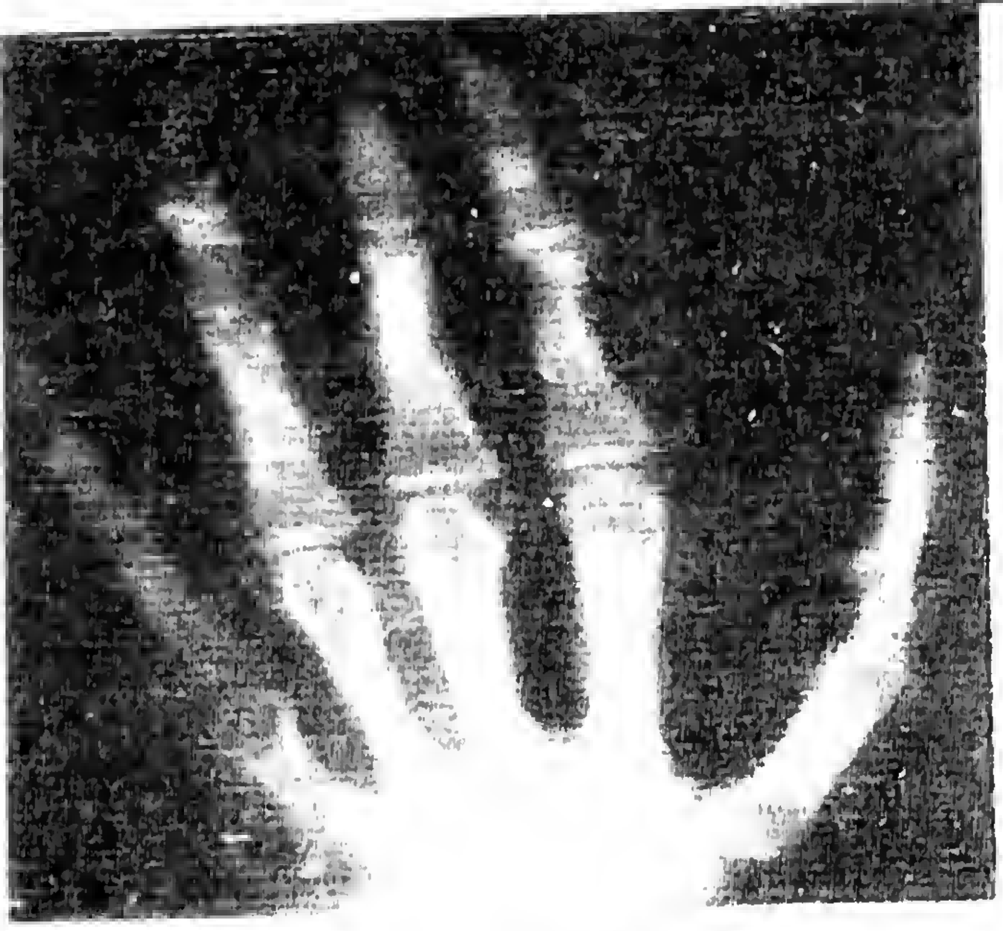

Fig. 1b

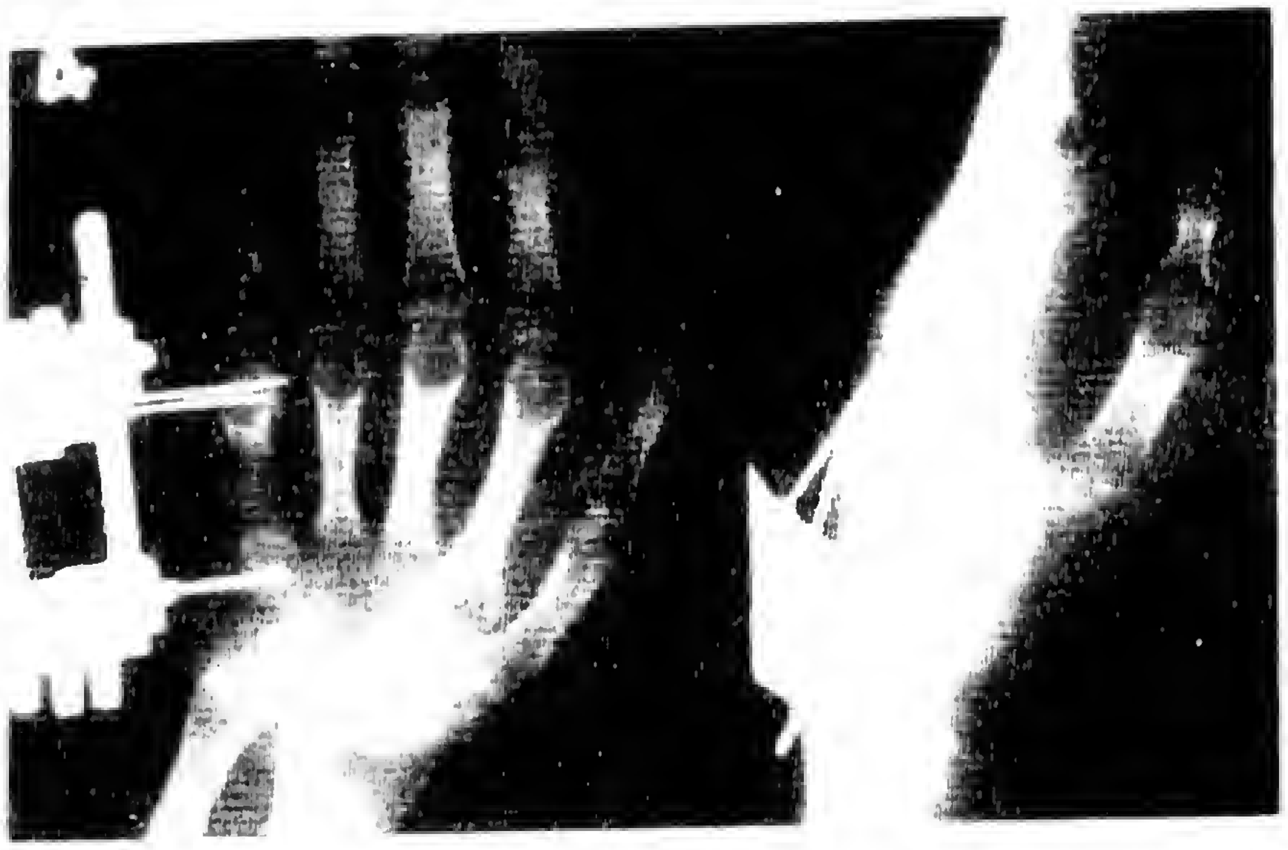

Fig. 1c

ROENTGENOGRAMS

1a. Shortening of Little fugr.

1b. Shortening of 5th metacarpal.

1c. Lengthening of 5th metacarpal.

1d&1e. Final Results (Clinical Photographs)

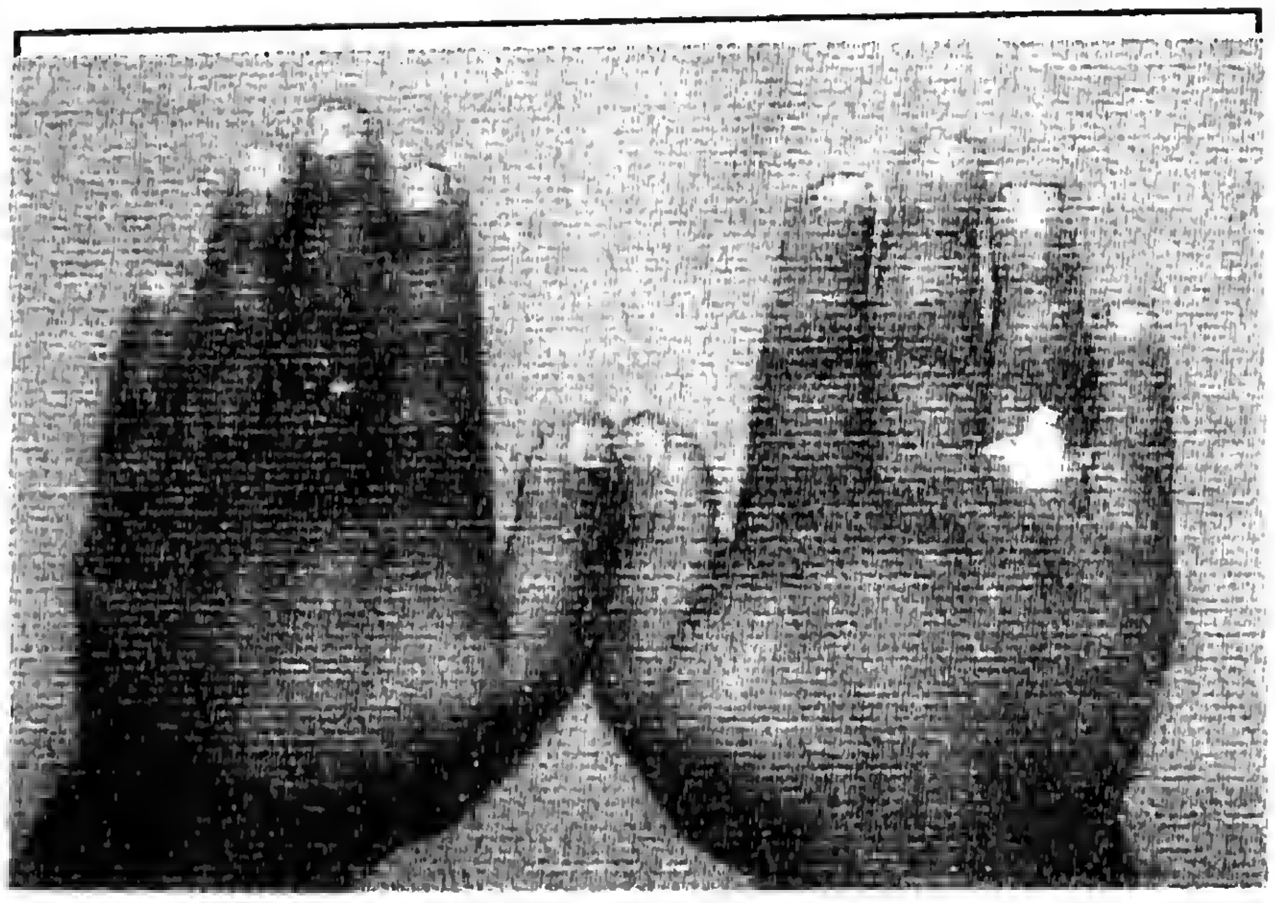

Fig. 1d

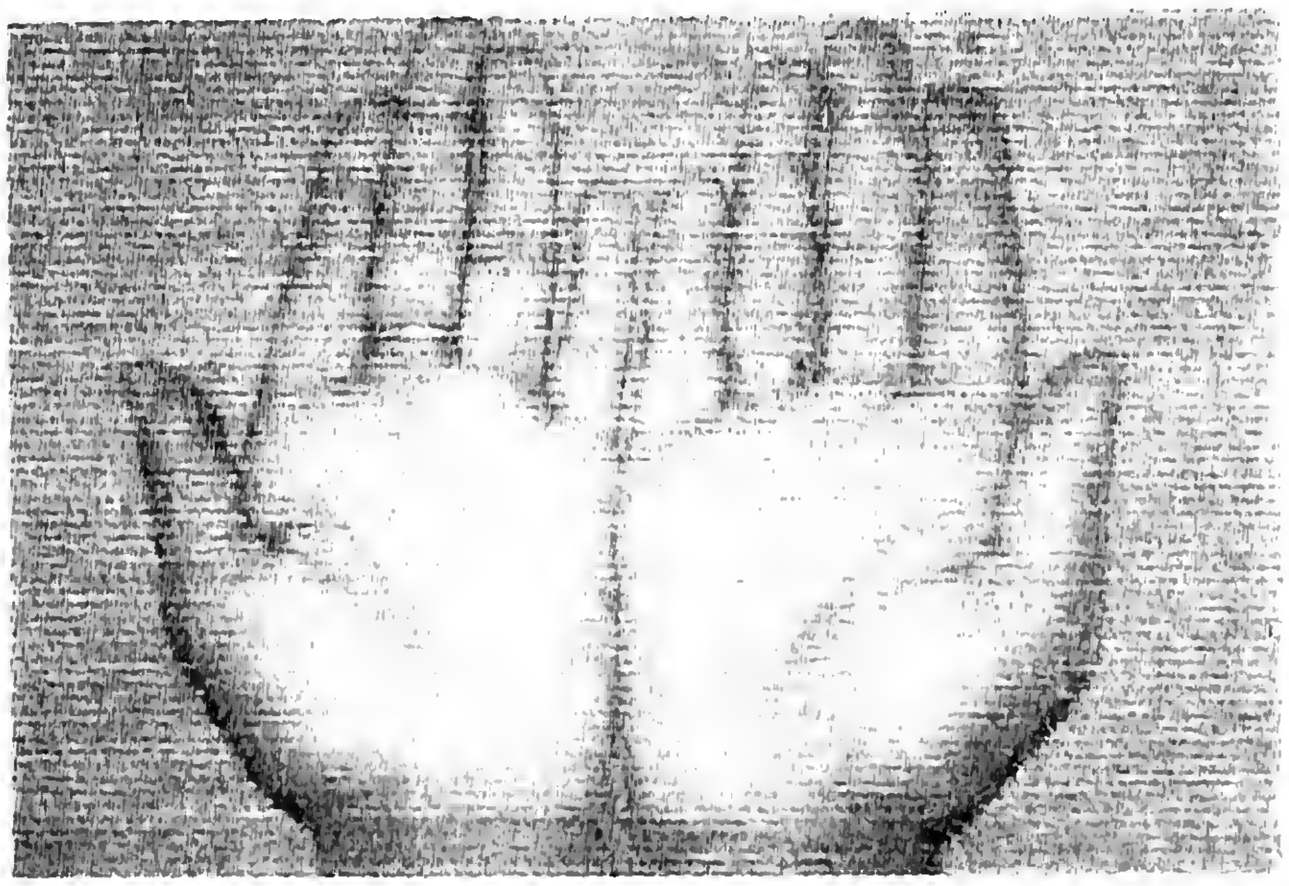

Fig. 1e

Table 1: Details fo the Patients

Patient No.	*Age*	*Metacarpal involved*	*Sex*	*Length achieved*	*Healing indes (months/cm)*	*Complications*
1.	20	Left little	F	25mm	1.2	Pin loosening, Pin tract infection
2.	15	Right middle	F	20mm	1.4	Pin tract infection
3.	17.	Right middle	F	17mm	1.4	Pin tract infection
4.	21	Left middle	F	28mm	1.5	Pain
5.	16	Left ring	F	23mm	1.2	Pain

Results:

All patients achieved the desired length and were happy with the aesthetic improvement of hand. The average length achieved was 23mm and the average healing index was1.3 months/cm. Two patients complained of pain during the initial days of distraction. This was managed by analgesics. Grade one pin tract infection in three patients was managed by antibiotics and local dressings only. In one patient one pin loosened after being caught in the dress. This was reintroduced under local anesthesia. There were no neuro vascular complications, no non-union and no refracture.

Discussion:

The role of distraction osteogenesis is now well defined in the management of congenital and acquired digital deficiencies and has proved to be more effective than replantation and toe transfers in certain conditions like the mangled hand, thermal injuries of hands, and in amputated digits with loss of amputated parts[1]. Furthermore the procedure provides original sensate skin covering and avoids cold intolerance and stiffness[1]. While the role of distraction osteogenesis is well defined in certain conditions, earlier studies question its use in isolated brachymetaoarpia where lengthening is performed for pure cosmetic reasons[2]. These studies stress more on the use of one stage lengthening and use of intercalary bone grafts to achieve the desired length. The single staged procedure of lengthening however may show graft resorbtion, malunion, circulatory disturbances, need for interna. fixation and is associated with pain and donor site morbidity[1,3]. Ogino T et al found satisfactory results in patients with brachymetacarpia where lengthening was performed for cosmetic reasons[3]. They believe that in presence of altenative methods, one stage lengthening procedures should be avoided. In our series of patients the lengthening was achieved with out any major complications. Mild pain in initial days of distraction and mild pin tract infection were not of a major concern and were managed with analgesics and antibiotics respectively. The amount of length achieved and the healing index in our series is consistent with other series[4,5,6]. Satisfactory results are also seen in the series of Arsalan H[7]. The amount of length achieved by distraction osteogenesis is greater than by one stage lengthening[3]. Miyawaki T et al in a 13-year period study found distraction osteogenesis to be more effective in terms of achieving adequate length[8]. Though the period of consolidation is higher than that of single stage lengthening in the literature, yet the ease of application of a very light weight minifixator, gradual lengthening without pain and avoidance of donor site morbidity seems to have definite advantages over single stage lengthening procedures[9]. More and more studies in the literature find it an effective technique and consider brachymetacarpia as an appropriate indication for callotasis[4]. Though our series is very small yet after reviewing the results in our series and other similar series' it is apparent that distraction osteogenesis is an easy and safe procedure for metacarpal lengthening.

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TECHNICAL DIFFICULTIES IN THE MOLECULAR DIAGNOSIS OF FOLLICULAR LYMPHOMAS

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Abstract: *The accent in this study is put on the association of the rearrangements of the bcl-2 gene with the follicular lymphomas diagnosis. Nine blood samples taken from patients diagnosed with follicular lymphomas were put to analysis. The phases of the molecular analysis were: the extraction of the total RNA, obtaining cDNA by reversetranscription, amplifying cDNA by PCR and showing of the amplification products by electrophoresis in agarose gel. The results obtained are corresponding with the data in the specialized literature; this method is expensive and difficult, but it is indispensable for the accuracy of the diagnosis and for evaluating the response of the treatment.*

Key words: *follicular lymphomas, bcl-2 rearrangement, t(14, 18), RT-PCR*

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Introduction

Proto-oncogene bcl-2 is localized on the chromosome 18 in the q21 region. Normally it encodes a protein with antipoptotic activity, which has a role in the prolongation of cellular life duration. Usually it is well represented in the embryo, but in the adult it is active only in the germ cells.[1]

Pathologic, it is implicated in the translocation t(14;18)(q21;q32) appeared as a bcl-2 gene superposition follow up in the chapter 5' of the union between the six JH segments of the heavy chains of immunoglobulins, localized on the chromosome 14 in the q32 region (fig.1). The rearrangements leads to the super expression bcl-2 which in turn determines the apoptosis suppression and the growth in the lymphocyte B pool which gets out of control of the programmed death. For this reason it is considered that t(14;18) is a cytogenesis marker and a molecular marker for the diagnosis of follicular lymphoma.

Regarding the association of the translocation with the diagnosis of follicular lymphomas, specialization literature communicates the results as being 100% in the United States, 85% in the Western Europe[2, 3, 4, 5] and 0-10% in Saudi Arabia.[6,7]

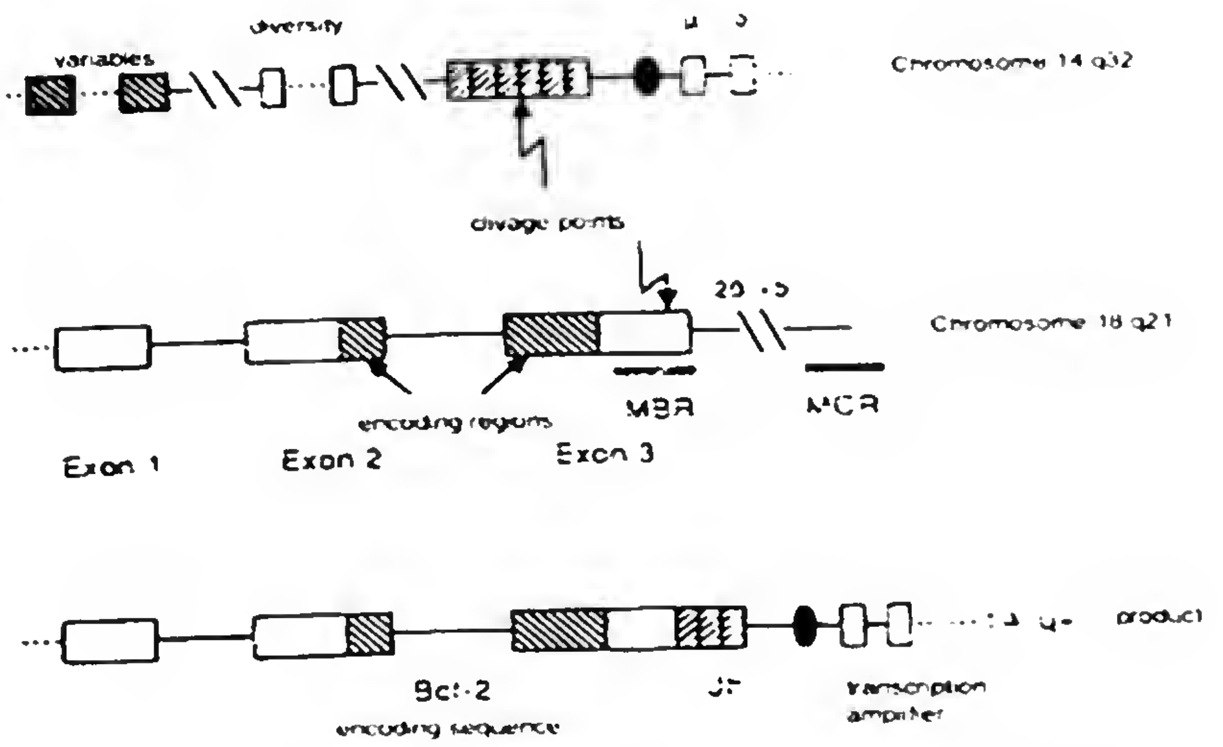

Fig. 1: Schematic Representation of the translocation t (14;18)[8]

Material and method

We undertook a study with clinical impact in which we used the RT-PCR technique for the bcl-2/JH fusion detection to a number of 9 ill adults, admitted in the Hematology Section of the Municipal Hospital Timisoara, who were diagnosed with follicular lymphomas. The molecular analysis was realized for every case at the time of admission, before starting the treatment and post treatment.

The steps that were taken are as follows:-

1. 2 ml of peripheral blood was taken using EDTA K3 as anticoagulant.
2. The isolation of the total RNA from 250 microliters of peripheral blood, using the phenol / chloroform method (reactive TRIZOL-Gibco).
3. cDNA synthesis from the reverse transcription (RT SUPERSCRIPT II-Invitrogene kit).
4. DNA amplification (Primeri Maxim Bio-Tech kit) with the Taq polymerase addition and using a thermocycler gene AMP 9600.
5. Migration of the amplificated product from gel

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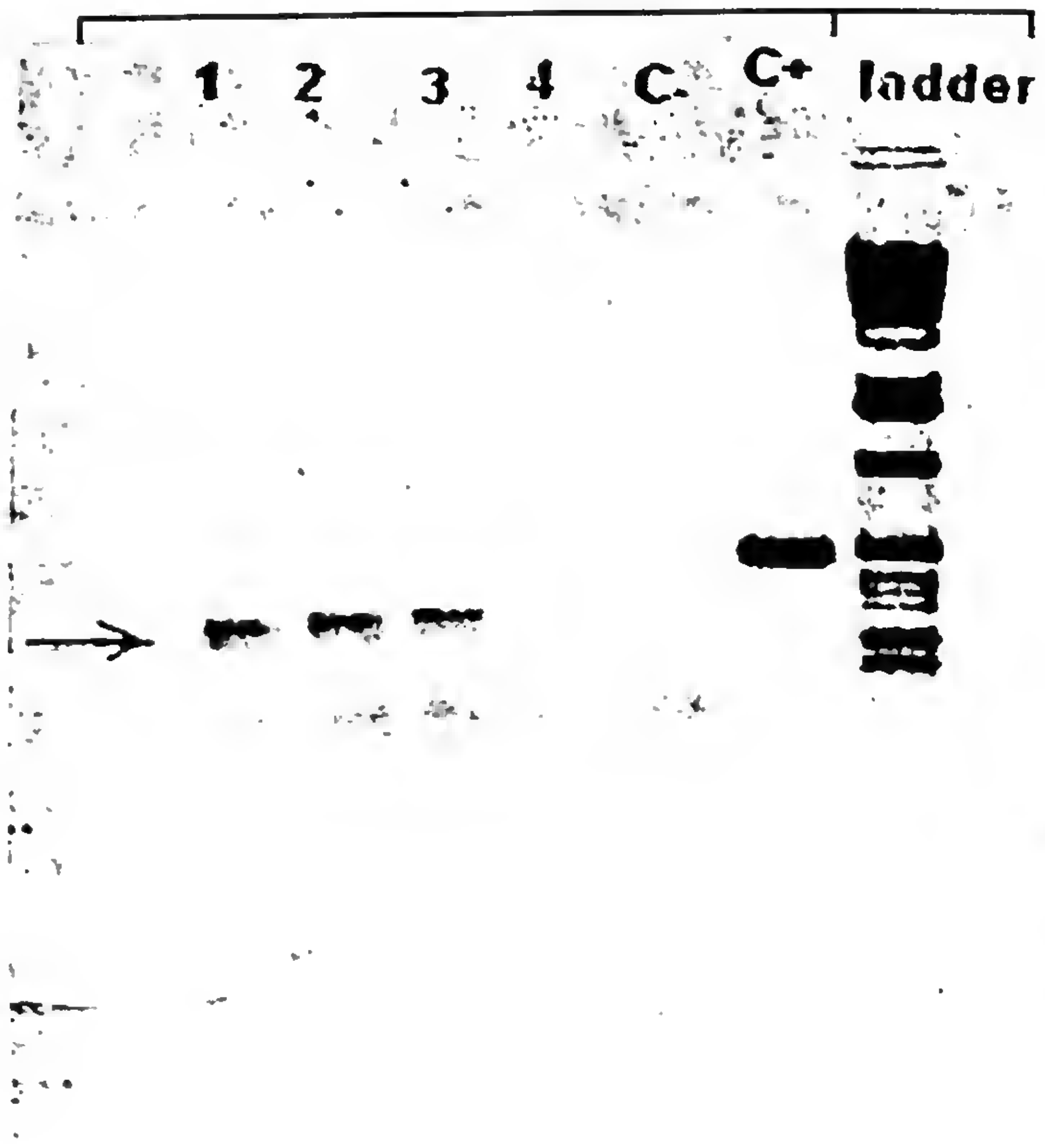

electrophoresis (agar 1% in TBE), using as fluorochrome a 1% solution of ethidium bromure.

6. Exposure in UV transluminator, computerized, recording and study of the results with the help of the "Quantity One" programme (fig.2)

Fig. 2: Amplification results - agarose gel 2%. 1,2,3 - Positive results; 4 - negative result; c - negative control C+ -RT positive control (500bp)

The study followed the use of one of the quality methods of evidence of supraexpression / nonexpression of the bcl-2 gene in the lymphocyte line cells, with a scope of offering the clinicians, initially a diagnosis of precision and then an assement of the response to the treatment prescribed with regard to the outcome of the patients. From this point of view the study attained the scope, because the molecular rearrangements of the bcl-2 gene, which were evident in 8 out of the 9 cases (88.8%) investigated at the time of admission and became negative post treatment.

The single case in which the modified gene was not evident belongs to the group of patients who got ill again, with a clinical symptomatology and the hematological analysis of the medium intensity, which can explain the lack of its detection. Regarding the association of the translocation with the diagnosis of follicular lymphoma, the study results are compatible with those in the specialized literature.

We met difficulties in all the steps of realization of the molecular analysis.

- RNA isolation with phenol/chloroform method leads to a final volume of the reaction of only 10 microliters, insufficient for verifying the concentration of the RNA in the test.
- PCR reaction is inhibited by persistence of a lot of impurities even if their concentration is very low, phenol, ethanol, isopropranol, EDTA, haemoglobin, mixture of the RT reaction."
- Addition of the entire product of reaction RT decreases the production of the PCR product. From repeated trying we obtained good results when the volume of the TR reaction transferred into the PCR mixture was 10% from the total volume of PCR.
- The primers with 0,2 micromoles concentration were used with a length of 20 nucleotides (clockwise) respectively 21 nucleotides (anticlockwise) in which the concentration of the CG was 65% and 52%. respectively The annealing temperature was calculated after the 2x (A+T) + 4x (C+G) formula. Even in these conditions, the migration results from the electrophoresis demonstrated a reduced annealing capacity, the concentration of the remnant primers being much more than that of the amplicons, fact that determined us to reform the thermocycler programme to other levels of temperature until we obtained the significant results. This fact demonstrates that each apparatus of amplification presents a specificity for obtaining and maintenance of temperatures to which they were programmed, the seconds in which it realizes "shoulder" curves being essential for the success of the reaction.

Conclusions

1. ***Method utility:*** according to the destination of the methods used, one can consider that:

   In the clinical scope, detection of the rearrangement of the bcl-2 gene is absolutely necessary for the accuracy of the diagnosis, and also for assesment of the response to the treatment and for evaluation of the prognosis in each case. The method can be extended also for the diagnosis of other forms of lymphomas with B cells, knowing the fact that the translocation of the bcl-2 gene does not limit itself to the follicular lymphomas. Translocation was also detected with a reduced frequency in other lymphoid tumors such as the big cell lymphomas, immunoblastic lymphomas, Hodgkin's disease: it can also be detected by PCR in the benign hyperplasia of the tonsils [3] and in circulatin B lymphocytes from normal blood of the donors. [4]

   In research scope, the balanced relation between the bax and bcl-2 genes can offer data regarding the regulation mechanism of the duration for the cell age duration, knowing the fact that the bax proteins accelerate the apoptosis, while the bcl-2 proteins inhibits it.

2. **Materials and methods of realization:** molecular analysis implies a large number of reaction stages, whose final results under optimal conditions depend on the used devices and kits:

- Clinical tests can contain substances that inhibit the amplification by PCR.
- The final extraction volume by the phenol / chloroform technique is insufficient if one follows the introduction of intermediate steps of verifying the total RNA contents by electrophoresis.
- The persistence of minimal levels of traditional reactive used for RNA extraction can inhibit the amplifying reaction.
- The RT reaction volume transfered into the PCR mixture can not surpass 10% of the total PCR charging volume.
- Every amplifying device (even if it has a similar production badge) can present specific realization conditions of temperature cycles, reason to the optimization for each primers set used.
- An increased ethidium bromure quantity and concentration used in the preparation of the gels can screen the visualization of the results especially when amplifying products are of small dimensions (100-300 bp).

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INCIDENCE OF NOSOCOMIAL WOUND INFECTION IN POST-RATIVE PATIENTS AT A TEACHING HOSPITAL IN KASHMIR.

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Abstract: *A prospective study of incidence of nosocomial wound infection and the microorganisms responsible in post-operative period at a large teaching hospital of Kashmir, revealed wound infection rate of 11.3%. Staphylococcus aureus was the predominant pathogen accounting for 70.5% of positive cultures, followed by Escherichia coli 29.5%. Nosocomial wound infection was observed higher in patients with a longer pre-operative (6.08 ± 4.37 days) and post-operative (9.06 ± 3.27 days) stay in hospital than patients having shorter pre-operative (5.02 ± 3.34 days) and post-operative (5.48 ± 2.28 days) stay. The study comprised of 150 patients in the age group of 20 years to 60 years from General Surgery ward with a male: female ratio of 1:2 who were operated electively.*

Key words: *Wound, Nosocomial Infections.*

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Nosocomial infections are those that develop within a hospital or are produced by microorganisms acquired during hospitalization. Infections incubating at the time of patient's admission to the hospital are not nosocomial; they are community acquired.[1]

Noscomial infection is one of the most important factors that adversely affect the performance and image of the hospitals. Besides morbidity and mortality, it prolongs the hospitals stay of the patients, increases bed occupancy rate and thereby puts undue pressure on the already strained resources of the hospital, patients, community and the country. Nosocomial infections may involve not only patients but also anyone else who has contact with the hospital inclouding staff members and visitors.[2]

In India incidence of post operative infections in various hospitals varies from 10-25%. Wound infection affects nearly 20% of post operative cases and there is evidence showing people rather than things as the most important aetiological factors. Nosocomial infection contribute upto 57% of extra hospital days and 42% of extra costs.[3]

Nosocomial infections invariably occur as a result of close environment where medical and paramedical staff is in close contact with the patient in various stages of treatment. It is very difficult to accurately pinpoint the source of infection. Nosocomial infections involve diverse anatomic sites, but the risk of these various types of infections and consequently their relative frequency appears to be similar in most hospitals[4].

Use of antimicrobial prophylaxis has been demonstrated in multicentre studies involving a large number of patients to bring about a significant reduction in the incidence of post-operative nosocomial infections[5,6]. Factors underlying nosocomial wound infections are multiple and include the type of surgical procedure, the skill of the surgeon, the duration of surgery, the type of anesthesia and the underlying diseases of the host, particularly his nutritional state, obesity and degree of immunological competence.[7]

Objectives:

The present study regarding nosocomial wound infections in post operative patients of general surgery ward was undertaken at Sher-i-Kashmir Institute of Medical Science (SKIMS) Srinagar- 600 bedded super-specialty hospital, with the broad aim towards generating data regarding incidence of nosocomial infections and their causative microorganisms to develop the hospital infection control policies and machinery which would serve as an information and decision making system for surveillance and control of hospital acquired infection in order to improve hospital productivity in qualitative as well as quantitative terms.

Material Methods

The study was undertaken on150 patients who were already on the follow-up in the surgical out patient department for cholilithiasis, carcinoma breast, gastric outlet obstruction, major surgeries involving removal of cyst and mass. These were taken up for elective surgeries, among these patients male:female ratio was 1: 2 the age range of

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20 years to 60 years having an optimal nutritional status belonging to different socio-economic status.

It was attempted that the study population represents patients from almost all physiographic regions of the valley and the patients were selected at random. However, this study was limited to the regional ethnic population. Care was taken to exclude those patients who were admitted for elective surgery in the pediatric or geriatric age group. Patients who had any clinical or microbiological evidence of infection like urinary tract infection, respiratory tract infection, gastrointestinal infection, dermatological infections or those who were using or had used antibiotics, corticosteroids, chemotherapeutic agents or immunosuppressive drugs on long term basis were also excluded.

After selected patients were admitted in general surgery ward and from time to time each patient was followed according to the protocol of this study. The relevant information was recorded during pre-operative, intra-operative and post-operative periods by using predesigned proforma respectively for each period.

During intra-operative period of said patients the ambient temperature inside theatre (degree C), humidity (%) and ventilation air changes per hour in theatre were recorded. Similarly storage and removal methods adopted for soiled linen were recorded. Swabs for culture were taken from walls, floor of operating suite; this was taken before the start of first case of the day in general surgery theare. Cultures were taken from operation table top and from dressing material before its use for patients; these swabs were taken to the department of microbiology for identification of pathogens. In the operation room it was observed during surgery if the staff adheres to the principles and practice of changing clean theatre dress and observing aseptic precautions.

For evry selected patient who had to undergo conventional surgery, minimal invasive surgery or laparoscopic surgery, the type of anesthesia (general, local or spinal) and the duration for how much time in minutes given were recorded. Actual duration of surgery and site of drain were recorded.

Post-operative period was the major area of focus of this study as any complication arising during this period would reflect upon the features and qualities of pre-operative and intra-operative care. Complications like fever, respiratory tract infection, urinary tract infection, gastrointestinal tract infection,etc. in general and local complications whatsoever at the operation and drain site were recorded by seeing the daily case summary and vital chart of patients.

For all the patients details of operation site were recorded including number of dressings changed at operation site and at drain site and whether the dressings were stained or not.

In chronological order the status of dressing in terms of frequency and soakage was recorded to know if dressing was done daily, alternately, every 3rd day or not all. In general surgery ward and its dressing room samples were taken randomly for antimicrobials from dressing material/ linen used on patients during dressing.

The data was collected using pre-designed proformas and questionnaires. The protested, standardized questionnaires were administered among various doctors of general surgery ward, nursing officers. Theatre technologists, officer in charge central sterile department, theatre sterile supply unit technologist, sanitation officer and sanitary supervisors to ascertain their level of awareness about aseptic precautions and factors contributing to nosocomial infections during pre-operative, intra-operative and post-operative periods.

The patients were followed till discharge routinely for vitals like pulse, respiration, temperature and specifically for any sign and symptom of wound infection. Data so collected was analyzed, tabulated and put to various statistical tests.

Results

The study revealed that the incidence of nosocomial wound infection in the post-operative elective surgeries was 11.3% i.e., out of 150 patients studied 37 developed infection. The microorganism found were Staphylococcus aureus 70.5% and Escherichia coli 29.5%. Our results are comparable with the hospitals of similar size overseas (Fig.1).

On analysis, the positive culture for different organisms did not show statistically sufficient difference in different socio-economic groups, among lower socio-economic group it was 14.7%, middle 10.3% and higher 10%.

Out of 191 cultures taken from different sites of operation theatre (during intra operative period) 19 cultures were positive for E-coli, Staphylococcus aureus and Klebsiella independent of site. The microorganisms responsible for post operative surgical site infection were same as found in operation theatre site culture in 63.5% of patients (Fig.2).

The post operative microbiological cultures were significantly positive in patients who had longer pre operative (6.88 ± 4.37 days) and post operative (9.06 ± 3.27 days) stay in hospital than patients having shorter pre operative (5.02 ± 3.34 days) and post operative (5.48 ± 2.28 days) stay.

The study revealed more number of positive cases (n = 12) in daily linen change group as against positive cases (n = 5) in alternate linen change group. Linen change as such may not be causative to the wound infection but the patients who developed wound infection received daily linen change.

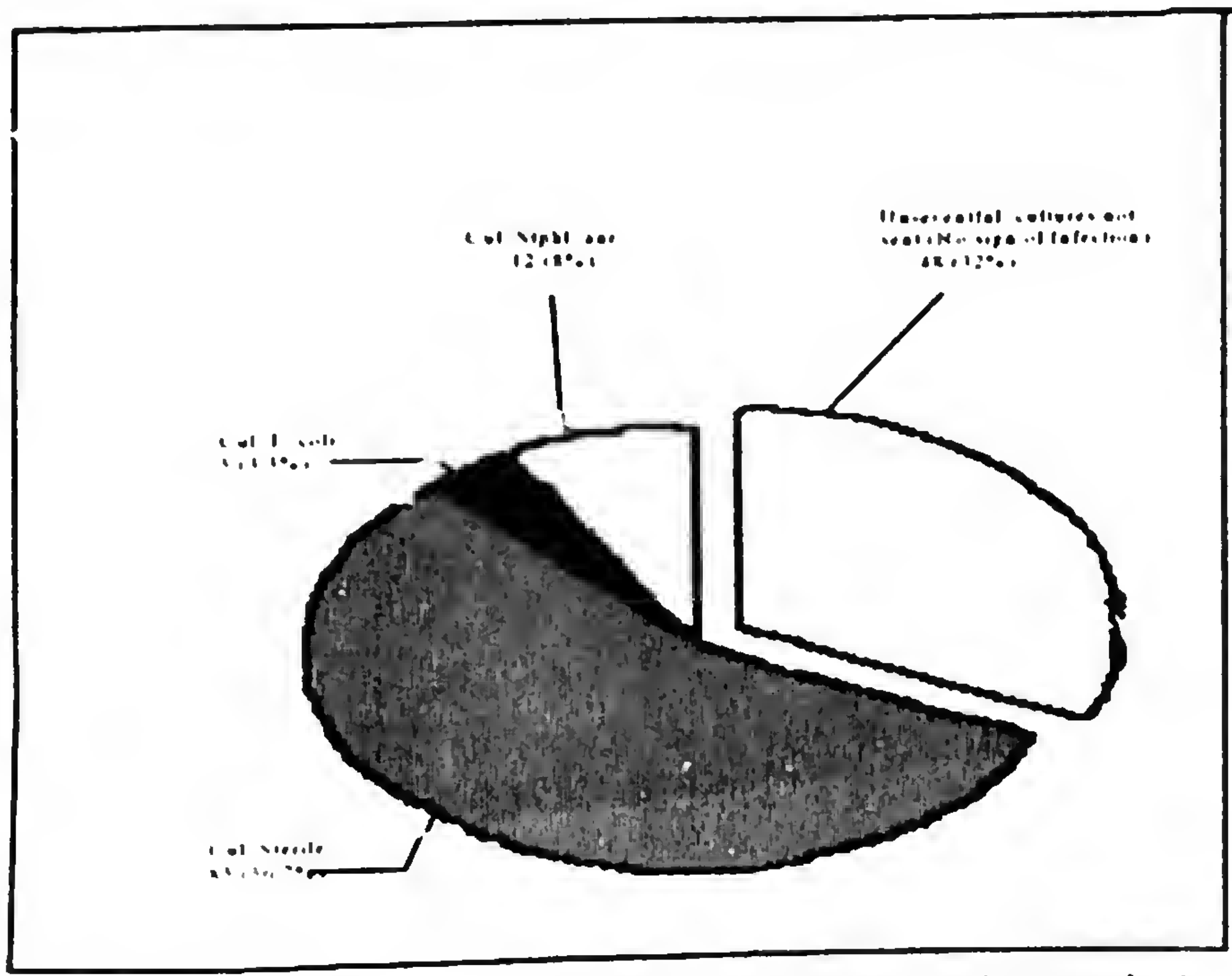

Fig. 1 Incidence of nosocomial infection at postoperative surgical wound site of 150 patients studied

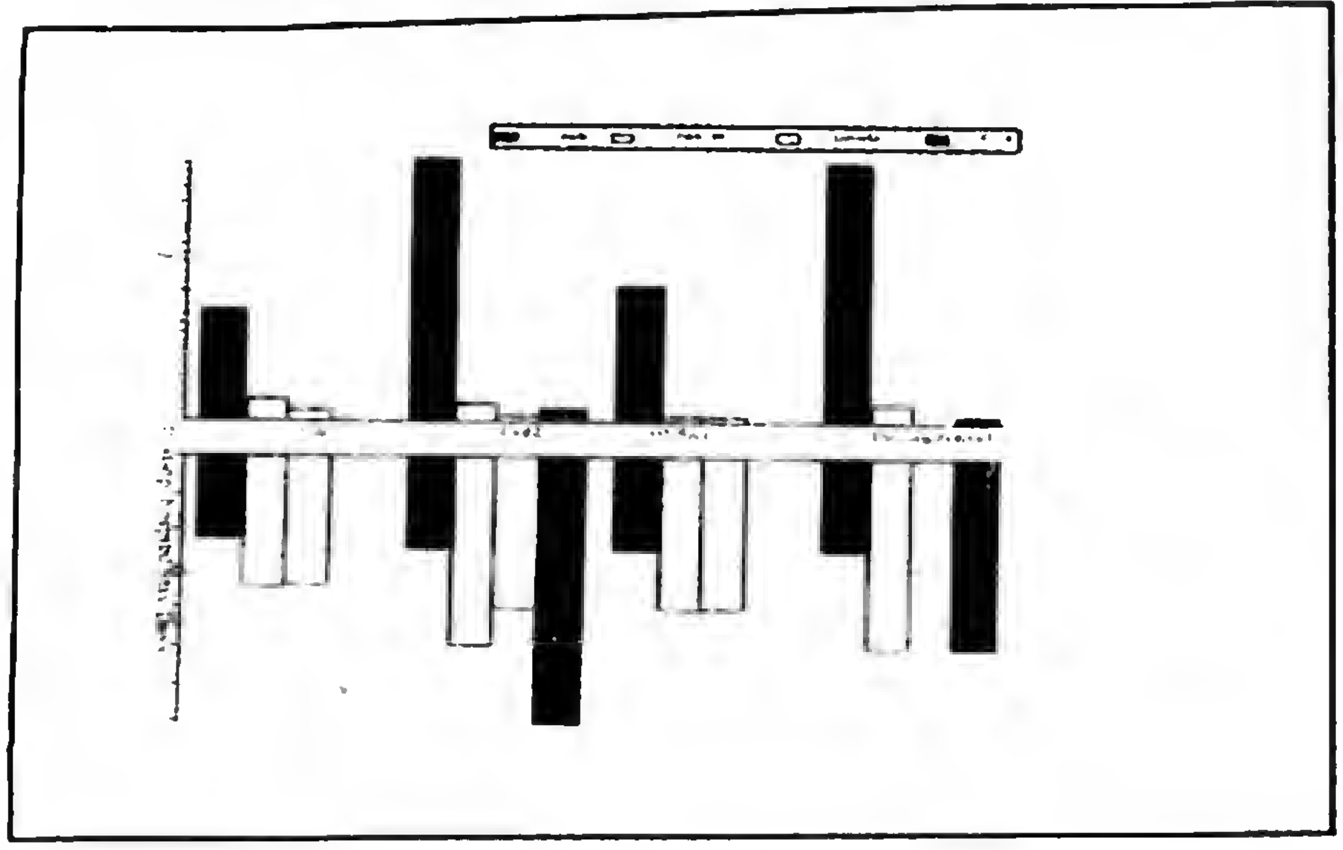

Fig.2 Effect of microbiological contamination of operation theatre wall.OT fable,OT Floor and dressing material on post-operative hospital stay

The study revealed that hand washing, post operative fever and signs of infection at the operation are related to positive microbiological cultures indicating interdependence of these factors for promoting nosocomial infection. Every person who works in a hospital is responsible for helping to prevent nosocomial infections. The least that every one can do is to keep his hands clean at all times.

Whether or not, prophylactic use of antibiotic can suppress the post-operative wound infection and reduce post-operative hospital stay, data was analyzed but no correlation was found. 143 received prophylactic antibiotics. 72 developed fever including 17 patients who were showing positive microbiological culture at surgical site. This indicates that prophylactic use of antibiotics may not have any significant role in preventing nosocomial wound infection. However, more data will be required to establish this observation.

Conclusion

Improvement in staff knowledge regarding nosocomial acquired infection is required in wards, kitchen, sanitation department, CSSD, Operation Theatre and Laboratories. The hospital administrators, the infection control committee, medical and nursing staffs must recognize that the ultimate aim of such programme is prevention of nosocomial infection and consequent improvement of patient care.

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CASE REPORT

UNILATERAL HYDROTHORAX COMPLICATING CONTINUOUS AMBULATORY PERITONEAL DIALYSIS A CASE REPORT WITH REVIEW OF NITERATURE

Mohd. Saleem Najar M.D.; Syed Sajjad Nazir M.S.; Baldev S. Wazir M.S.; Mohd. Ashraf Bhat M.D.; Khursheed Banday M.D.

ABSTRACT: Increased intraabdominal pressure can result in leak of dailysis fluid across the diaphragm and into the pleural space. The accumulation of dialysis fluid in the pleural cavity is called Hydrothorax. It is not clear how often hydrothorax occurs in patients receiving peritoneal dialysis, but most studies estimate that incidence range from 1.6 % - 2.9 %, although actual frequency may be much higher because low degrees of hydrothorax may pass un-noticed. Hydrothorax can occur any time during the course of peritoneal dialysis, is more common in females and tend to occur on right side. This condition is serious, although generally not life threatening. We present a case who developed right sided hydrothorax after one year of peritoneal dialysis.

Key words: Continuous ambulatory peritoneal dialysis, hydrothorax, pleural space, peritoneal fluid, dialysate.

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CASE REPORT

A 55 year old female patient diagnosed, case of CRF due to CGN, and on continuous ambulatory peritoneal dialysis for last one year, presented to us with sudden onset of dyspnea , compromised ventilation and decreased dialysate volume return. Physical examination revealed BP 140/90mmHg, RR 36/mt, shallow breathing, HR 120 / min, pale and in distress. Chest on auscultation showed absent breath sounds on right side with stony dull on percussion and vocal vibration not transmitted. Abdomen was soft non-tender, non distended and CAPD catheter found in place. A provisional diagnosis of salt/water retention with expansion of extracellular volume, heart failure and hypoproteinurea was kept in mind. Investigations done revealed as: ABG- respiratory acidosis, Na- 133, K- 5.4, Cl- 102, Urea- 105, Creatinine- 8.6, Hb- 7.5, TLC- 7600, DLC- L65, L_{30} E_{05}, Alb- 3, Total protein- 5.2, SGPT, OT- Normal, Bilirubin- 0.8, Calcium- 8.4, ECG- Normal, X-ray Chest P/A view and lateral view revealed Rt. sided massive hydrothorax.

Treatment

A intercostal chest tube 32 No. was put in 5th ICS from rt. side in emergency O.T. and about 2.5 litres of fluid drained. This fluid was send for analysis and revealed high glucose (>40mmol/L) low protein transduate fluid with no other cells seen. After putting chest tube, patient's ventilation improved and we again started peritoneal dialysis the next morning. While patient was receiving PD and when about 2.0 litres of dialysate went in, fluid was seen coming out through the chest tube, which had stopped draining early, thus suggesting a pleuro-peritoneal communication. A temporary transfer to hemodialysis for 4 weeks was performed, after obtaining vascular access through a Radial A-V fistula and peritoneal dialysis stopped for 4 weeks. Chest tube was removed as soon as patient was shifted to hemodialysis. After 4 weeks of hemodialysis, peritoneal dialysis was resumed with a higher number of lower volume exchanges and also keeping patient in a semi sitting position. This patient is doing well and we have now increased the volume of exchange. Earlier 4 months back, patient had developed staph. peritonitis due to external cuff extrusion, which was treated with inj. vancomycin and removal of external cuff of the catheter and since then patient never had any further episodes of peritonitis.

Discussion

Hydrothorax associated with abnormal communications between the peritoneal and abdominal cavities was first described by Meigs, who reported the existence of pleural effusion and ascitis associated with ovarian fibroma [1]. Likewise, Ratnoff quoted by Popper, gave one of the first descriptions of hydrothorax as a complication of ascites associated with liver cirrhosis [2]. Since then, various authors have approached the study of "Hepatic hydrothorax [3-9]. Recently, several cases have been reported associated with ovarian stimulation[10].

As a replacement therapy for chronic renal failure, peritoneal dialysis involves the abdominal instillation of a variable volume of dialysis solution, giving rise to an "Artificial ascitis". The common denominator of all cases of hydrothorax that have been reported is the presence of

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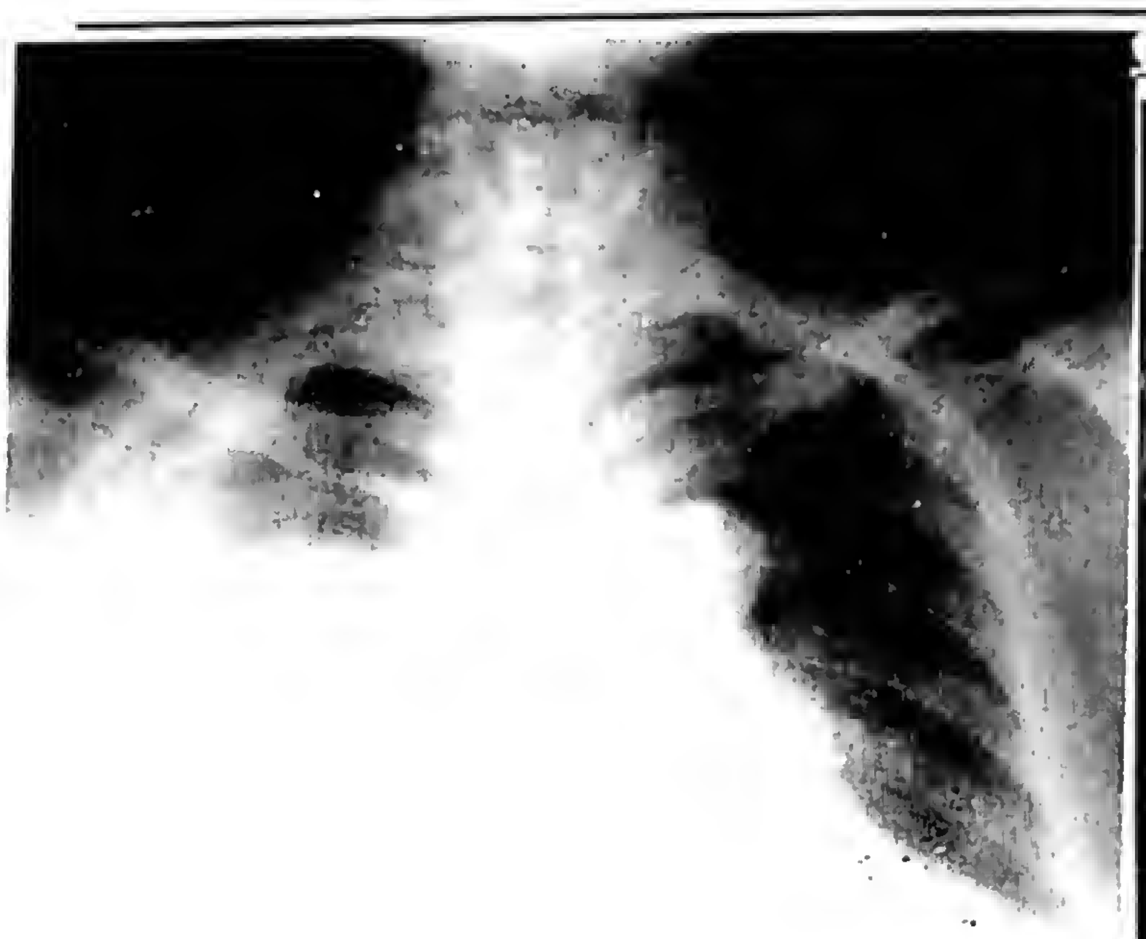

Fig. 1.: X-Ray P/A view of the Chest Showing right sided pleural effusion.

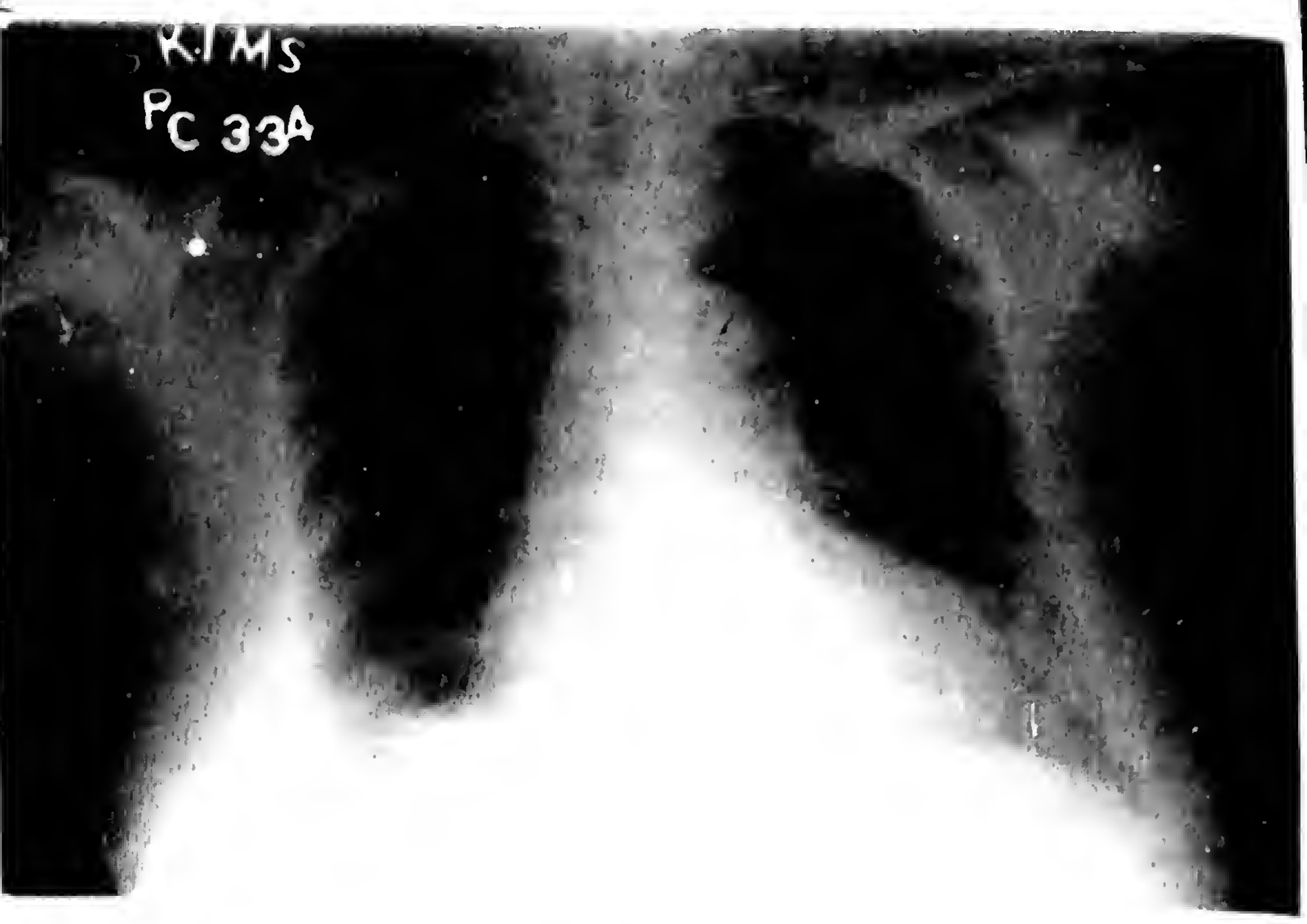

Fig. 2.: X-Ray P/A view showing chest tube on right side with resolution of effusion.

fluid in the peritoneal cavity combined with an increase in hydrostatic pressure. The first descriptions of this complication are credited to Edward, Unger, Finn and Jowett in the 1960's [11,12]. Since then, others have reported such cases and examined different aspects of this complication[13-21]. The prevalence of this complication varies, ranging from 1.6% in Nomoto et al's series, which reported 50 cases of hydrothorax in a population of 3195 PD patients[15] 2.9% in the series studied by Shemin et al [16]. Its prevalence is similar to that of hydrothorax observed among cirrhotic patients with ascitis but without renal failure[6,7,24] This complication is serious, although generally not life threatening and on many occasions, it forces the patient to withdraw from peritoneal dialysis and to accept a temporary or permanent transfer to hemodialysis[11-21,23,24]. It has been described much more often in women[11-14,20] although only 46% of Nomoto's patients were women. It develops chiefly in the right hemithorax, indeed 88% of Nomoto's cases where in this location[15].

The most common presentation is immediately after starting PD or a few days later, although cases have been described with a longer latent period, even several years[15,24], as in our case, patient presented after one year. Sometimes, it is asymptomatic and is detected accidently in a routine chest X-ray. In some cases the patient reports only a decrease in ultrafiltration, which indicates that dialysate is collecting in the pleural space. On other occasions, the hydrothorax presents with sudden onset dyspnea and compromised ventilation that requires thoracocentesis as in our case. Less common symptoms are pleuritic chest pain, weight gain and hypotension.

A prominent predisposing factor cited in the literature is polycystic kidney disease, because the kidney's volume decrease abdominal capacity and the subsequent infusion of dialysate increases the Hydrostatic pressure[25]. In some instances, the condition appeared after coughing fits[26] or in association with tight girdles worn for reasons of fashion[27].

Autopy studies have revealed localized absence of muscle fibres in the hemidiaphragm[7,8]. The missing muscle fibres are replaced with a disordered network of collagen. One or more defects in the tendenious part of the hemidiaphragm have been observed[7,8,18,19]. Assuming that such defect exists, the mechanism behind the hydrothorax is simple. The physiological negative pressure in the pleural space and the increased positive pressure in the peritoneal cavity caused by the presence of fluid favour the passage of the fluid along the pressure gradient, thereafter, the fluid will remain in the pleural cavity until the gradient disappears. This mechanism explains the development of massive hydrothorax shortly after starting dialysis and the remission observed after stopping peritoneal dialysis, as the pressure gradient has been eliminated. Other authors believe that the passage of fluid is one-way, from the abdomen to pleura, either because of a valve defect or due to the temponade action of the subphrenic hepatic capsule[20]. In contrast, there are patients who develop hydrothorax months to years after starting peritoneal dialysis suggesting an acquired mechanism such as a constant increase in inter-abdominal pressure that causes small discontinuites due to the breakage of collagen fibres in the diaphragmatic pleuroperitoneum, this action gives rise to small "bubbles" that within a weakened tissue, can break, allowing communication between the two cavities[8,15,19,20,24,28] or an episode of peritonitis to remove the barrier between the two cavities, as in our case. Another mechanism that has been postulated, is lymph drainage disorder, particularly in the right hemidiaphragm, where the system is most abundant[8,2830].

For diagnosis chemical characteristic of the pleural fluid should be compared with the patient's blood. It has the charactereristics of a transduate with a low protein content <30-35g/L. Pleural LDH levels are low and glucose content is high, similar to dialysis fluid and higher than the patient's blood sugar level even if patient is diabetic. This is not evident in small hydrothorax or in the instances where the evacuation of pleural fluid has been delayed, because the glucose is reabsorbed via pleural membrane[28,31]. Some authors recommend the assessment of D-lactate in the sample, because the agent is a buffer in the dialysis solution and not found in the body[24]. Consequently, many carry out peritoneography with traditional iodinated contrast (Hypaque, Sanofi-Winthrop, NY, USA) and later non-ionic, isotonics iodinated contrast (Lopamidol). While these substances do not damage peritoneum[32], their diffusion is low. Methylene blue can be instilled in the peritoneal cavity before the peritoneal tap and blue staining of the pleural flow provides evidence of peritoneal-pleural communication. In addition to giving false negative, this technique is not without risk because in some patients, it can provoke chemical peritonitis[31] or side-effects related to the dye itself (e.g. general reaction, fever, malaise)[33].

The currently preferred technique uses radionuclides such as macro-aggregate of 99TC added to the dialysis bag at a dose of 3-10 mCi. This provides more accurate information about the existance of pleuroperitoneal communication and sometimes the precise location of the abnormal communication, while preserving peritonium . However, its reliability is not absolute[31,34-38].

Thoracocentesis is recommended for the immediate treatment of Hydrothorax if respiratory compromise is present. Otherwise, simply discontinuing peritoneal dialysis often leads to rapid and dramatic resolution of the pleural effusion[15,20,39,40]. Spontaneous resolution of these hydrothorax has been reported[30].

If a temporary transfer to hemodialysis is possible, the peritoneal dialysis is stopped, the patient remains on hemodialysis for approximately four weeks. Subsequently, peritoneal dialysis is resumed with a high number of lower volume exchanges, as in our case. Sometimes the patient can be put on automated peritoneal dialysis, which produces lower increases in intra-abdominal pressure. Some have suggested that the dialysate itself could act as a sclerosant by promoting a "waterproof seal" of the epithelial layers[24,41]. Inspite of occasional spontaneous resolutions, cure rates are about 40%[42] and recurrences are common.

In contrast to this "wait and see" attitude, one may choose such interventionist procedures such as pleurodesis; adhesion of the pleural using irritants instilled into the pleural cavity (chemical pleurodesis), by pleurectemy, or by mechanical abrasion of the pleurae. Among the most common of these substances have been asbestos-free talc[43], tetracyclines[44], fibrin derivatives such as tissucol with two components: fibrinogen and factor XIII, plus an aprotinin-thrombin solution[45], Nocardia rubra cell wall skeleton[46] and OK-432[47] and more recently, autologus blood obtained from a peripheral vein[48-51] ,. With these procedures , PD is stoped for about 4 weeks- the time thought to be needed for permanent fibrosis and the obliteration of the abnormal communication and if necessary, the patient is transferred to hemodialysis. At the end of the period, peritoneal dialysis is resumed with small volumes that are gradually increased. However, in spite of this, the failure rates after pleurodesis are high[42].

The most medical approach, used in recurrent cases or sometimes as first approach if the patient's general condition is good enough, is surgical repair with thoracotomy, which requires G/A[19,42,52,53]. The defects are located, sutured and can be reinforced with prosthetic material such as Teflon[42]. Sometimes, the bubbles in the tendenious hemidiaphragm are so small that they are difficult to identify.

With regard to the variability of the results, in their series, Nomoto et al reported that stopping peritoneal dialysis alone or in combination with pleurodesis achieved a 50% success rate; the reminder of his patient were transferred to hemodialysis[15]. After reviewing Nomoto's report, four studies published between 1982 and 1991, and isolated case reports[15,17,39,44,54] a total of 81 episodes and many different treatments. Allen and Mathens[42] reported that 56 patients who received conservative therapy, 30 were not relieved of their hydrothoraces and were transferred to hemo dialysis (53%); of 23 patients treated with pleurodesis, 10 were not relieved (43%) and subsequently, 2 patients treated with surgery, the hydrothorax disappeared. The results obtained with conservative therapy, and even with pleurodesis, casts doubt on the efficacy of these techniques.

In the case of eventration of the diaphragm, as reported in the pediatric literature, surgical repair can be affected by plication with nonabsorbable suture. These patients are able to return to peritoneal dialysis successfully[53].

Conclusion

Hydrothorax is a well described but relatively uncommon complication of peritoneal dialysis. Diagnosis is relatively simple once the possibility of peritoneal-pleural communication has been entertained. Thoracocentesis may be necessary to confirm the diagnosis and is mandated by respiratory embarrassment. If the patient is willing to continue with peritoneal dialysis, several treatment options are available.

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SPONTANEOUS PERFORATION OF RECTO-SIGMOID COLON: A REPORT OF 3 CASES

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Abstract: *Spontaneous perforation of recto-sigmoid colon is rare and mainly occurs as a complication of pathological conditions, such as diverticular disease, carcinoma,colitis, blunt or penetrating trauma and intra-luminal injury from faulty instrumentation*[1]*. Three cases of spontaneous perforation of recto-sigmoid colon are reported here.*

Key words:*Spontaneous, Perforation, Recto-Sigmoid colon.*

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Introduction:

Spontaneous perforation of the sigmoid colon or rectum is rare. The perforation is often associated with a sudden increase in intra-abdominal or intra-luminal pressure during defecation . The distinctive mechanisms are still unclear and many factors such as pressure necrosis, constipation, colonic dysfunction and ischaemic lesions have been suggested as risky factors. Increased pressure and local ischaemia might play an important role in the development of spontaneous perforation. The perforation occurs almost always in the distal part of the colon because of the physiological characteristics of recto-sigmoid colon, such as lower water content of the stool, relatively poor blood supply and high pressure due to the narrowed intra-luminal diameter.There should be no history of any injury, however trivial, prior to onset of the presenting symptoms in order to diagnose spontaneous perforation of the large bowel. Keeping in view the rarity, interesting clinical and radiological findings, we describe three cases of spontaneous rupture of recto-sigmoid colon.

Case-1

A 59-year-old man was admitted in casuality room with signs and symptoms of septic shock and diffuse peritonitis. Patient gave history of sudden abdominal pain 18- hours prior to admission and did have long standing history of constipation. The abdominal pain increased gradually but persistently and was accompanied by abdominal distention. On examination abdomen showed signs of rigidity with rebound tenderness. Bowel sounds were diminished. Plain X-ray abdomen showed free air in the sub-phrenic areas. An emergency exploratory laparotomy was carried. Peritoneal cavity was full of purulent fluid and faecal sediment was found in the lower abdomen. About 5-cm perforation was present over apex of the sigmoid colon. Biopsy was taken from the edge of the perforation and loop of sigmoid colon was taken out, along with the perforated site, as loop colostomy. The remainder of the large bowel looked normal.Post-operatively, he had respiratory tract infection with wound infection. He recovered from severe situation but developed incisional hernia and was discharged after 32-days of stay in hospital. After three months, the continuity of the bowel was restored. Incisional hernia was repaired with Prolene mesh placement. Biopsy showed non-specific features. He is doing well after more than 18 months of follow up.

Case-2

A 45-year-old male was seen in casualty with complaint of sudden lower abdominal pain for last 10 hours. He denied any history of bleeding per-rectum, external trauma to the perianal region or to the abdomen and excessive straining during defecation. His vital signs were stable but lower abdomen was tender and rigid. X-ray examination showed free air in bilateral sub-phrenic spaces. Emergency exploratory laparotomy was performed through lower midline incision. Peritoneal cavity was contaminated with faecal matter and purulent fluid. A 4-cm perforation of the anterior wall of the rectum just above the peritoneal reflection was found. Biopsy was taken from the edge of the perforation. Perforation was closed in single interrupted layer and a proximal sigmoid colostomy was constructed after thorough peritoneal toileting with saline. Biopsy showed necrosis with infiltration of inflammatory cells. The patient recovered smoothly, being discharged uneventfully 15-days after the operation. The continuity of the bowel was restored three months later. One year after the operation, he is still doing well.

Case-3

A 55-year-old male was referred from a peripheral hospital with pain and distension of abdomen. On examination patient was febrile, dehydrated and dyspnoeic. The whole abdomen was tender with board like rigidity. Bowel sounds were absent. Standing x-ray abdomen

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showed gas under diaphragm. After adequate hydration and correction of electrolyte imbalance patient was taken for emergency laparotomy. On operation, peritoneal cavity was full of purulent fluid and faecal matter. Small and large bowels were congested. A 4-cm perforation was found at the anti-mesenteric side of the sigmoid loop. Biopsy was taken from the edge of the perforation. Loop of sigmoid colon was exteriorised along with the perforated site as colostomy. Post-operatively, patient did well and had uneventful recovery and was discharged after 18-days of stay in hospital. The continuity of the bowel was restored after 4- months. Biopsy was non-specific. He is doing remarkably well after 10 months of follow-up.

Discussion:

Spontaneous perforation of the sigmoid colon or rectum is rare[1]. The perforation is often associated with a sudden increase in intra-abdominal or intra-luminal pressure during defecation[2,3]. The distinctive mechanisms are still unclear, and many factors such as pressure necrosis, constipation, colonic dysfunction and ischaemic lesions have been suggested as risky factors[2,4,5]. The voluntary contraction of abdominal muscles may be accentuated in the presence of resistance in the rectum, and further increase the intra-luminal pressure and the risk of rupture[2, 3, 6].

Increased pressure and local ischaemia might play an important role in the development of spontaneous perforation. The perforation occurs almost always in the distal part of the colon because of the physiological characteristics of recto-sigmoid colon, such as lower water content of the stool, relatively poor blood supply and high pressure due to the narrowed intra-luminal diameter[2]. The literature indicates that the typical sites of spontaneous perforation include the anterior wall of the rectum just proximal to the peritoneal reflection, the anti-mesenteric border of the recto-sigmoid junction and the apex of the sigmoid loop[7]. It was true in our cases.

There should be no history of any injury, however trivial, prior to onset of the presenting symptoms in order to diagnose spontaneous perforation of the large bowel[8]. It was true with our cases.

Brodie (1827) described the cases of middle-aged women whose rectums suddenly ruptured, apparently spontaneously[8]. Since then, there have been about 64 published cases of spontaneous rupture of the colon and rectum. These cases comprised 36 males and 28 females. Their ages ranged from 16 to 96 years (mean 56 years), and more than half of them were less than 60 years of age. In 58%, perforation was in the sigmoid colon, in 16%, the perforation was in the recto-sigmoid junction and rectal perforation was found in 26% of cases. In all these cases perforation was on the anti-mesenteric border[9]. Prior to 1961, the mortality of those who underwent closure of the perforation only was much higher (80%) than those who had in addition colostomy or exteriorization of the site of perforation (20%)[9]. In our cases, all were males, treatment included closure of perforation with proximal colostomy or exteriorization of the bowel along with the perforated site and all are doing well.

The treatment of spontaneous recto-sigmoid perforation is almost the same as that for other recto-sigmoid perforations. It is very important to recognize the condition at an early stage and treat it by surgical intervention with appropriate antibiotics. Recto-sigmoid perforation should always be suspected when a patient with chronic constipation presents with severe abdominal pain. In patients diagnosed early, simple closure may suffice; in patients diagnosed late, it may require exteriorisation or colostomy[10]. Although closure of the perforation without colostomy is an acceptable procedure in cases diagnosed early, we believe a totally defunctioning colostomy should be added to the procedure in accordance with the principles of treatment of traumatic perforation of the rectum[9,11].

Conclusion:

Spontaneous perforation of the recto-sigmoid colon is a rare surgical entity and when it occurs, it calls for an immediate intervention. The treatment consists of preparation of the patients for the exploratory laparotomy, thorough peritoneal toileting, antibiotics, closure of the site of perforation and proximal loop colostomy or only exteriorization of the site of perforation.

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PRIMARY PULMONARY NON-HODGKIN'S LYMPHOMA

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ABSTRACT: Primary pulmonary malignant tumours are very rare in children and in this group non-Hodgkin's lymphoma are probably the rarest. We report two patients from a tertiary care centre with primary pulmonary non-Hodgkin's lymphoma and review the literature .

Key words: Non-hodgkin's Lymphoma, Lung.

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INTRODUCTION

Most pulmonary neoplasms in children are caused by metastatic disease, but primary tumours of the lungs also occur in children. Plasma cell granuloma is the most common benign tumour in children, but the most frequently encountered malignant pulmonary tumour is bronchial adenoma. Carcinoid tumours account for 80 to 85 percent of all bronchial adenoma in children. Primary lymphoma of the lung are rare and an incidence of as low as 0.33 percent to 0.5 percent has been reported among all lung tumours. However, primary pulmonary non-Hodgkin's lymphoma is a very rare entity. We report two cases with review of literature.

Case reports

Patient 1

A 7 years old girl was admitted for the management of reported hemothorax. She had presented with features of right pleural effusion at a district hospital, since she drained more then 400 ml blood after the thoracostomy she was referred to our centre. Examination of the patient revealed severe pallor with features of atelectasis of right lung. CT scan chest revealed soft tissue enhancing mass replacing literally the whole lung with significant adenopathy. Bronchoscopy was of no help except for compression of upper lobe bronchus. CT guided aspiration and bronchoscopic lavage for cytology was inconclusive. Except for lung functions, CBC and x-ray chest all other test such as liver function, kidney function, coagulogram, panendoscopy, USG abdomen and CT skull were normal.

An exploratory thoracotomy was attempted because haemorrhagic drainage continued, but only the tissue from the mass could be taken for biopsy, frozen section revealed features consistent with lymphoma and histopathological examination revealed non-Hodgkin's lymphoma large cell type. The patient died in postoperative period secondary to DIC.

Patient 2

A 8 year old boy presented with features of fever, breathlessness, cough, easy fatiguability and sweating. Examination of the patient was consistent with right sided pleural effusion. The boy was under treatment of a paediatrician for URTI from last 10 days. He had a skiagram chest done 10 days back(Fig. 1) and a repeat skiagram chest done 1 day back (Fig. 2). He was referred to our department as a case of ruptured hydatid cyst lung. The patient was evaluated in detail. CBC, liver, kidney functions, coagulogram, urine and blood cultures were normal. USG abdomen were normal. Skiagram chest showed destruction of 2nd rib in addition to complete opacification right side. CT scan chest showed soft tissue enhancing mass replacing whole of right lung with hilar adenopathy. Trucut biopsy was done and the tissue obtained for histopathological examination. The biopsy report was consistent with features of non-Hodgkin's lymphoma.

OBSERVATION

Both the patients presented with features of respiratory tract infection, had rapid progression of disease. Clinically the patients were very sick with features suggestive of malignancy at least with certanity in one. One had destruction of the rib CT findings were similar in both. Both the patients had locally advanced disease at presentation one patient died in peri-operative period.

REVIEW

Commonly encountered uncommon primary malignant

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tumours of the lungs are sarcomas. Most pulmonary neoplasms in children are caused by metastatic disease, but primary tumours of lungs also occur in children. The approximate ratio of primary pulmonary tumour to metastatic neoplasm to non-neoplastic lesion of the lung is 1:5:60.[1] The most frequently encountered malignant primary pulmonary tumour is a bronchial adenoma.

Primary pulmonary lymphomas constitute only about 0.33 to 0.5 percent of malignant tumour. In a reported series of 151 primary pulmonary malignant tumours there were three cases of lymphoma, and all the three were non-Hodgkin's type.[2] Of the three two were managed with pneumonectomy and irradiation and one with irradiation alone. In another series of 291 patients with primary pulmonary neoplasm in children, 3 patients had pulmonary lymphoma.[3] In contrast, of the reported 80 rare pulmonary neoplasm from Mayo clinics 41 percent were non-Hodgkin's lymphomas, 20 percent carcinosarcoma, 15 percent mucoepidermoid carcinomas, 18 percent sarcomas and the remainder were either malignant melanomas or blastomas.[4] The median age in their patients was 60 years. As regards the percentage of rare pulmonary neoplasms in Children, bronchial adenoma, bronchogenic carcinoma, pulmonary blastoma, fibrosarcoma, rhabdomyosarcoma, leiomyosarcoma, sarcoma, hemangiopericytoma, plasmacytoma, lymphoma, teratoma, mesenchymoma and myxosarcoma constituted 40.5, 16.8, 15.5, 9.6, 5.8, 3.8, 2.1, 1.4, 1.4, 1.0, 1.0, 0.7, and 0.3 percent respectively[2]. Although primary pulmonary non-Hodgkin's lymphoma is very rare in children yet it is a well documented disease entity, these tumours represented 0.5 percent of all lung tumours.

The primary pulmonary lymphoma may occur in any of the deposits of lymphoid elements normally present in the lung such as bronchial associated lymphoid tissue, interstices of the lung parenchyma, intrapulmonary and subpleural lymphnodes. Primary pulmonary lymphoma develops from B lymphocytes predominantly. Symptomatology clinical examination and investigative procedures and management has been established from last more than two decades new[6-8]. The management in both our cases differed. In the first patient formal thoracotomy was done and patient died in perioperative period by the time histopathological examination was available. The second patient responded to chemotherapy and their was significant decrease in tumour volume.

Since we had only two case reports and no long term follow up available no guidelines can be suggested, but we do emphasize minimally invasive surgical procedures/ early chemotherapy in all the patients where there is suspicious documentation of primary pulmonary lymphoma.

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POST- TRAUMATIC SUBDURAL WITH VENTRICULAR PNEUMATOCELE: A CASE REPORT AND REVIEW OF LITERATURE

Syed Sajjad Nazir M.S.; Mohd Afzal Wani M.S., M.Ch.; Altaf Rehman Kirmani M.S.

Abstract: *Pneumocephalus is usually defined as the presence of air in the intracranial cavity. It may be caused by a variety of processes including head trauma, infection, neoplasm or surgery involving sinuses, orbits, nasal passages or intra-cranial infections or tumors. The majority is due to trauma. Frontal region is the most vulnerable site and most common, accounts for about 93.33% of cases. Subdural pneumatocele is the commonest type while pure ventricular type is rare and is usually associated with subdural (as in this case) or subarachnoid type. Pathophysiology involves two mechanisms, Bale valve and Inverted bottle mechanism and in both situations there has to be a craniodural defect. While "succession splash" is considered pathognomonic, diagnosis is made radiographically by CT Scan. The therapy is usually conservative, as craniodural defect heals sponstaneously and only in selected cases immediate operative repair of the defect is required.*

Key words: *Pneumocephalus, Trauma, CSF leak, Subdural, Cranio Dural defect.*

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INTRODUCTION

Pneumocephalus results mostly as a complication of head trauma. It occurs in 0.5-0.88% (with male predominance) of head trauma. Although it may also occur as a complication of infections, neoplasms or neurologic surgery. Subdural pneumatocele is the commonest type of the pneumocephalus while pure ventricular pneumocephalus is rare and is usually associated with the subdural (as in this case) or subarachnoid type. In pathophysiology one of the two mechanisms are believed to take part in the formation of pneumocephalus. First a ball valve mechanism, in which air enters the cranium but does not exit. Second an inverted bottle mechanism, in which CSF leak permits air entrance as fluid leaves the intracranial space. In both situations there has to be a craniodural defect. While a 'succession splash' is considered pathognomonic of pneumocephalus. The diagnosis is made radiographically by CT Scan. The therapy is usually conservative, as craniodural defect heals spontaneously. Only in selected cases immediate operative repair of the defect is required.

Abnormal presence of air within the cranium is an uncommon entity usually caused by head trauma. Pneumocephalus may exist in a variety of intracranial spaces, depending upon the underlying cause. There are non-specific signs and symptoms. A physician should have an high index of suscipion in case of patient with a recent head trauma, nasal or orbital or ear trauma presenting with headache, CSF otorrhea, CSF rhinorrhea, motor paresis or the characteristic 'succession splash' (Bruit hydro aerique). Succession splash is a splashing sound heard by the patient due to motion of fluid wave in a gas filled space (like air within a bottle) and is considered pathognomonic of pneumocephalus.

Reported is a case of right frontal subdural pneumatocele with left ventricular pneumatocele which presented after 4 weeks after a road traffic accident with untreated depressed fracture of right frontal bone.

Case Report

A 50 years old man presented to the Accident and Emergency department of Sher-i-Kashmir Institute of Medical Sciences, Srinagar (India), complaining of headache (mostly frontal), recurrent vomiting, lethargy, light headedness, loss of appetite and watering from nose. Patient also complained of neck pain and generalized body aches and pain. He denied fever or chills and rigors and had experienced no weakness of any part of the body, ataxia, visual disturbances, bleeding from ear, & throat. However there was bleeding from nose at the time of injury impact. There was nothing significant in the medical history in the past or in family. One month back patient had been admitted in a peripheral hospital after sustaining head injury in a road traffic accident. He was given first aid treatment at the peripheral hospital and was referred to Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir (J&K) India as a case of depressed fracture (r) frontal bone with CSF rhinorrhea. He had received 16 capsules

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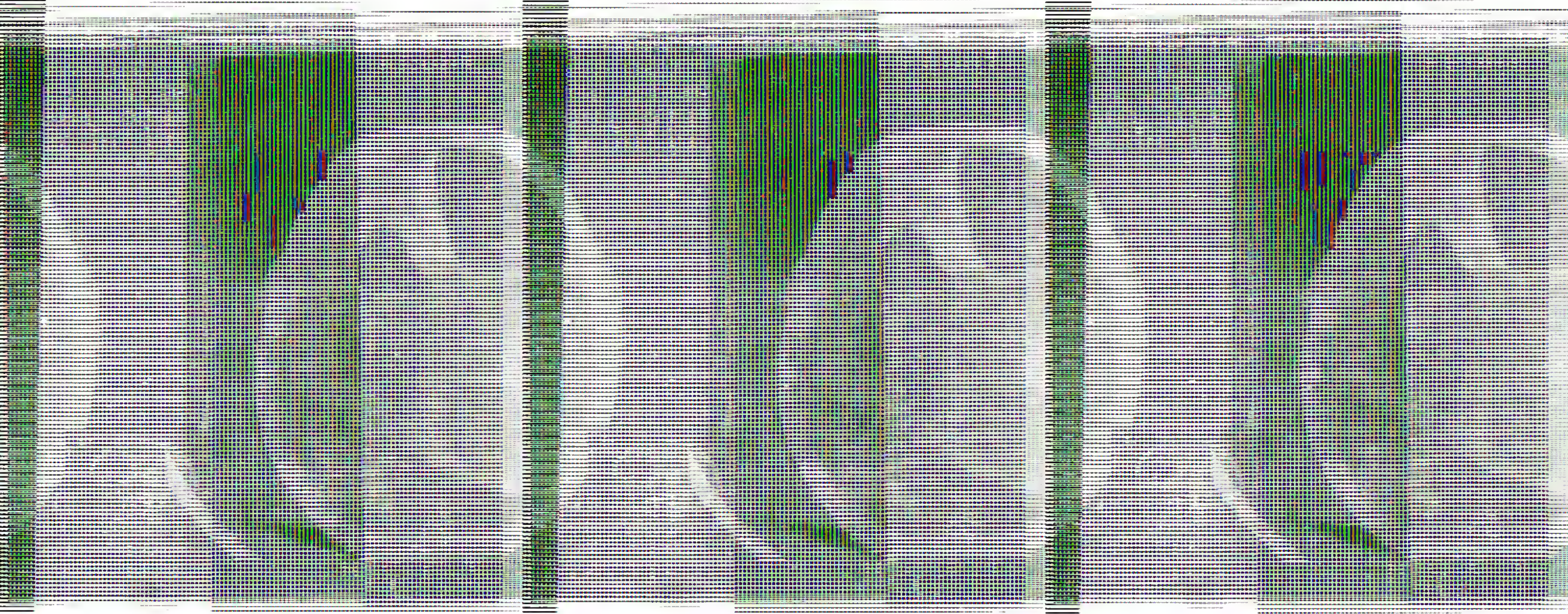

Fig. 1.

[illegible]

arachnoid membrane in proximity to a craniodural defect[6,7,8]

The pathophysiology of pneumocephalus usually involves one of the following two mechanisms. 1) "Ball-valve mechanism", there is a cranial defect adjacent to a point where air is available , as in cranio sinuses fracture , and air may be forced intracranially by coughing, sneezing, nose blowing etc. Once the air pressure wave has passed the dural defect, the opening is sealed due to a tamponade effect by pia-arachnoid and cerebral cortex, trapping the air mass intracranially. If this sequence of events occurs repeatedly, larger accumulation of air occur in the subdural space or within brain itself, giving rise to neurological signs, common to any space occupying lesion. This may also result in marked midline shift. This is referred to as "Tension" pneumocephalus and may result in herniation syndromes [12] Prompt decompression is essential [13] 2) "Inverted bottle mechanism" in which CSF leak permits air entrance as fluid leaves the intracranial space. Several other pathophysiologic mechanism exist; Director pressure wave. as occurs in penetrating cranial wounds due to missles, fragments etc. often result in the admission of at least a small amount of air into the cranium. Brain abscesses containing gas forming organism (clostridia + frankles bacillus) may result in intracranial gas collection. Finally cases of air introduction during lumber puncture have been reported [14]

Signs and symptoms are non-specific and quite minor, but occasionally may be serious, depending upon parenchymal injury present. In Markhams study presenting signs and symptoms were as follows; 43% complained of headache, 30.8% as CSF rhinorrhea , 9% had evidence of motor paresis and 8.1 % as seizure disorder. 3.4% had CSF otorrhea and 7% complained of succession splash [3].

The interval between injury and onset of pneumocephalus may vary from a few hours to 17 month; peak incidence is from one to three month in those cases due to trauma or due to neoplasms, and from one to four weeks due to infections. In missles injuries, pneumocephalus is diagnosed from 1 hr to 6 days after injury [8,14]. CSF rhinorrhea is the most common sign found in those with traumatic pneumocephalus, as a common pathophysiology underlies both pneumocephalus and rhinorrhea; a fistula traversing cranium, dura and arachnod[15] Such dural fistulas with CSF leak most commonly result from fracture of the delicate cribriform plate [16].

Other physical findings in pneumocephalus may include tympany on percussion of the skull and papilledema noted on fundus exam. Neurologic symptoms and signs may reflect intracranial hypertension or focal parenchymal compromise. Headache, lightheadedness or confusion may dominate the clinical picture, or one may detect subtle weakness, reflex abnormalities, a grasp reflex or frank hemipanesis [5,15,17,18]. Frontal lobe involvement often manifests a paucity of specific signs and symptoms.

The diagnosis of pneumocephalus is usually established radiographically. CT has replaced all other modalities, as the modality of choice for delineation of the location extent, and etiology of intracranial or intracerebral air. Intracranial air on CT scan is represented by areas of very low attenuation bordered by a white rim resulting from reconstruction artifact. This imaging modality is extremely sensitive, and can identify as little as 0.5cc of air in the intracranial spaces [1] Thus the CT obtained to rule out an intracranial hematoma or contusion will reveal even very small quantities of air, providing evidence of a basilar skull fracture. With CT imaging, air in the epidural space appears as a biconvex collection of gas not changing with movement. Subdural air tends to outline the contour of the skull and moves with a change in position of the head, although usually confined by the falx and tentorium Subarachnoid pneumocephalus appears on CT as non-confluent gas pockets conforming to the sulci and cisternal spaces, or the ventricular system. Air collections within the brain appear as round or oval intra-axial gas collections surrounded entirely by parenchyma. They may be seen to communicate with a sinus. At times, pneumatoceles will communicate with the ventricular system, and an air fluid level is evident [5,19,20] Regardless of location, intracranial air identified in a recently traumatized individual should alert the physician to the presence of basilar skull fracture and its consequences.

The therapeutic approach to traumatic pneumocephalus is similar to that for CSF fistula. Initial therapy is usually conservative, including head up position, avoidance of maneuvers which might increase intra-sinus pressures (such as nose blowing or valsalva maneuver) and prophylactic antibiotics [4] The risk of meningitis has been reduced considerably when prophylactic antibiotics are used, and those should cover pneumococcus and other gram positive organism [21,22] Most meningeal tears will seal spontaneously within one week, but 15% will not; necessitating surgical repair [20] Other situation in which surgical treatment is indicated include recurrent pneumocephalus, substantially depressed skull fracture, and the development of tension pneumocephalus. As in any serious head injury , consideration should be given to prophylactic anticonvulsants, depending on the extent of parenchymal trauma.

The consequences of overlooking pneumocephalus include progression to tension pneumocephalus and development of meningitis. The former is uncommon except in association with neurosurgical procedures. Most deaths in the setting of pneumocephalis are the result of meningitis[4]. In the preantibiotic era, the incidence of meningitis exceeded 50%, but has declined to 10% in the

Ist week after trauma, on those receiving prophylactic antibiotics [22]

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A CASE REPORT OF OF CONGENITAL TRIGGER THUMB

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Abstract: *The aetiology of trigger thumb in infancy and childhood is controversial. Many describe it as an acquired anomaly but there is some evidence that the condition may be congenital.*

We describe a case report in which two siblings were known to have this abnormality at birth. This observation suggests that at least in some cases the abnormality is congenital in nature.

Key Words: *Congenital Nodule, Trigger Thumb.*

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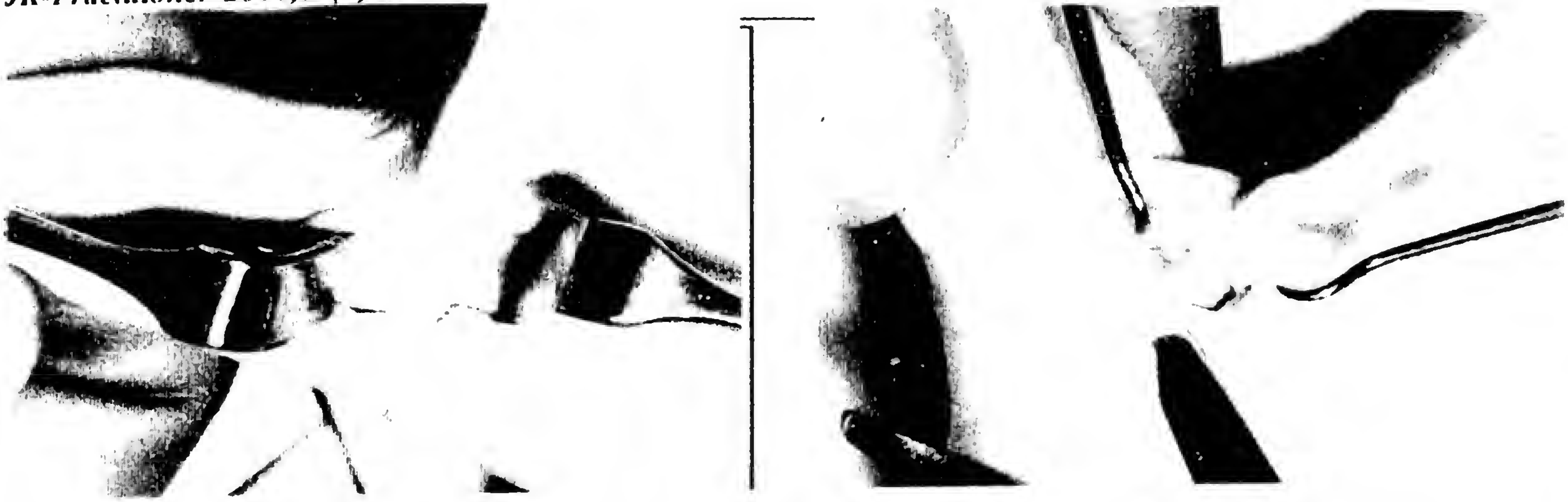

Fig. 1 & 2 Peroperative Photographs Showing thickening of Flexor Sheath over the tendon.

Case Report:

The flexion deformity of the thumb in our patient was noted by the parents when she was born as their older child had presented with a similar condition. She was first seen in the clinic at the age of five months when a palpable nodule was present over the flexor tendon of the thumb at the level of the metacarpo-phalangeal joint and it was possible to feel the triggering, when the thumb was passively extended. No specific treatment was recommended at that time. At two years of age the thumb presented with a fixed flexion deformity and she was therefore admitted as a day case for a release of the flexor pollicis longus tendon.(Fig 1-3)

Discussion:

Notta in 1850 first described triggering of the thumb and also noted a palpable thickening of the flexor tendon ("Notta's nodule").[1-5]

The aetiology of trigger thumb is still uncertain. The congenital nature of the condition has been supported by some researchers[2,3,5] but a few, larger studies conclude that the deformity is acquired or developmental[1,6,7] and described the term congenital as a misnomer.[7]

Triggering in a new-born has never been confirmed but in our case, since the parents were aware of this condition from their experience with the older sibling they specifically looked for and found this abnormality at birth. It is further confirmed by photographs of both siblings at five months of age. (Fig 4).

This case therefore strongly suggests that a congenital abnormality accounts for some instances of flexion deformity. The tendon sheath was thickened when exposed at operation although there was no adherence of the sheath to the tendon. (Fig 2)

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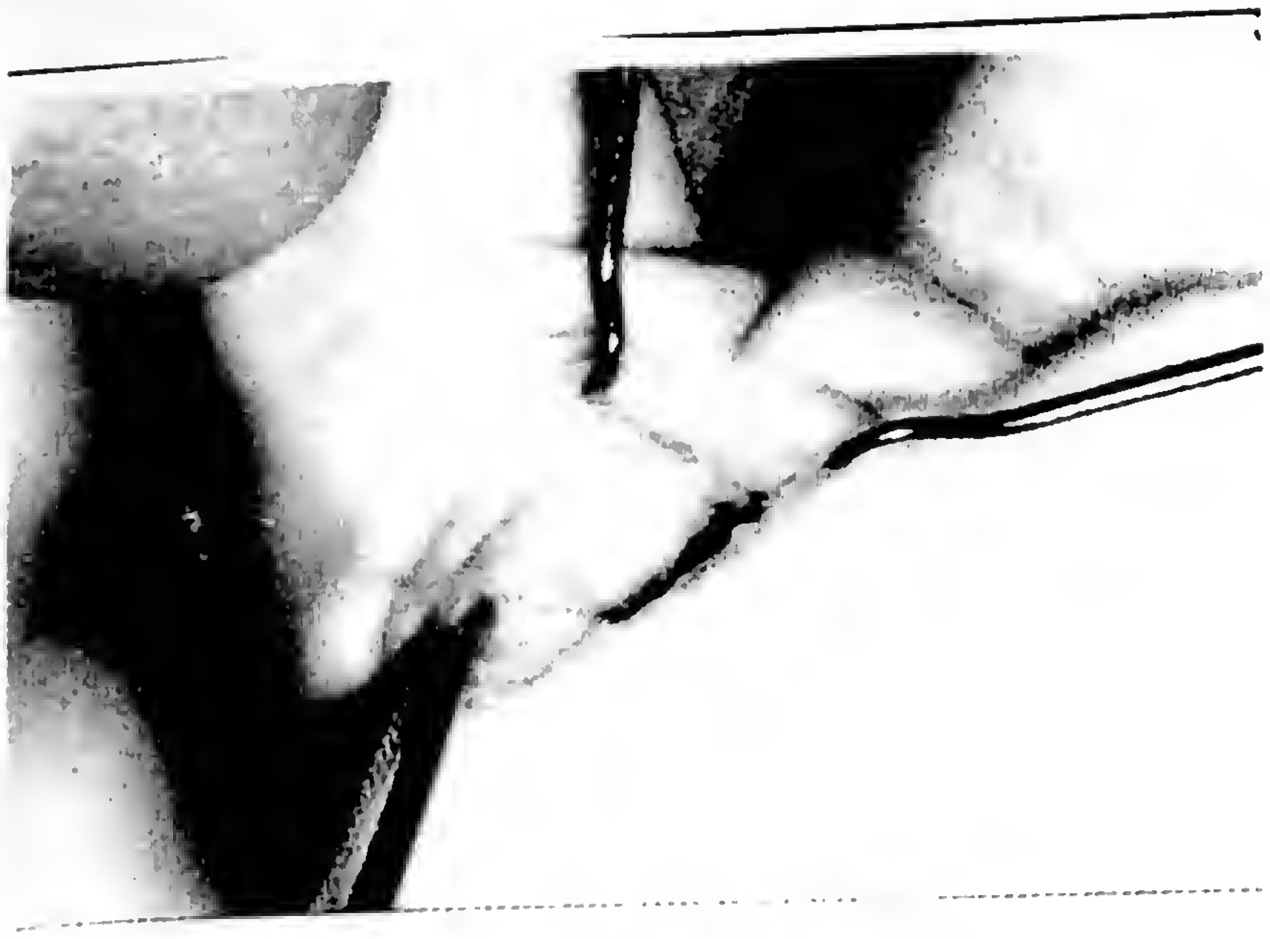

Fig. 3

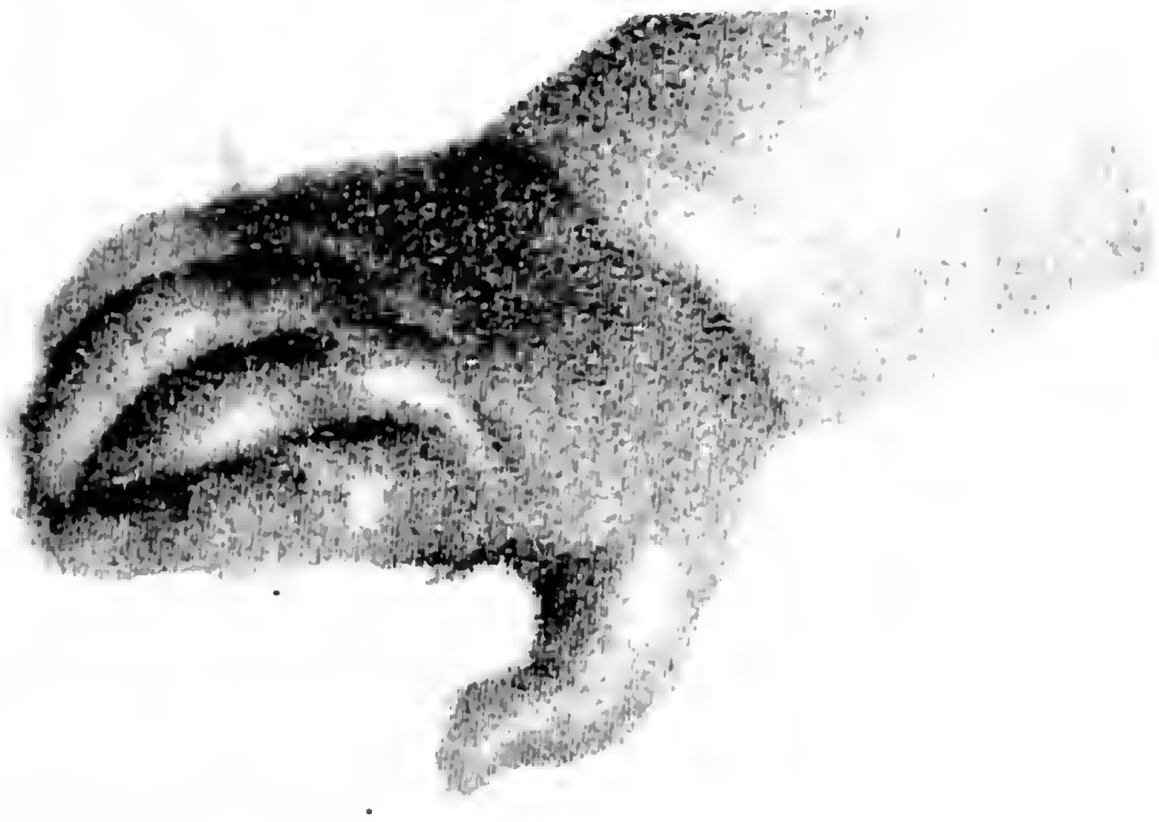

Fig. 4A

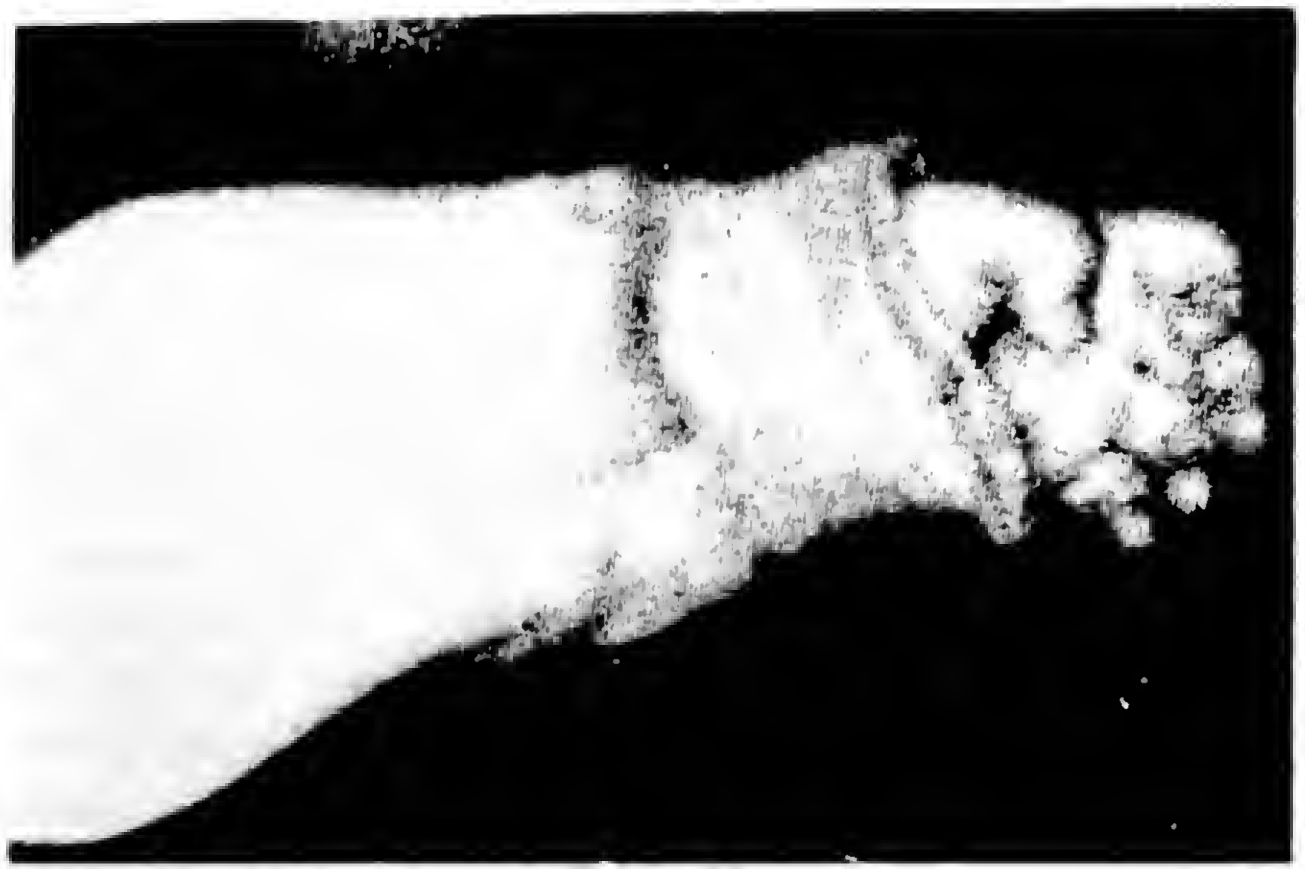

Fig. 4B

Fig. 3: ***Peroperative Photograph. After decompression tendon constriction noticed followed by a small swelling of tendon, but no adhesions.***

Fig. 4: ***Five months of age, clearly demonstrates flexion derformity of IPJ right thumb in patient (A) and sibling (B)***

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MAXILLOFACIAL BULLET INJURY

M. Latief; Masood A K; Talib Khan; K. Jeet Singh

Abstract: *The maxillofacial bullet injuries are usually lethal due to close proximity to the vital structures but a case presented here in which patient has escaped injury to vital structures and who was successfully managed by surgical exploration and removal of bullet, from the left maxillary antrum. The role of rigid fibro-optic endoscopy can't be ignored.*

Key words: *Maxillofacial bullet injury, Missile injury, bullet, vital structures, and surgical exploration.*

Abbreviations: *Kinetic energy (KE), computer topography (CT), under all aseptic precautions (UAAP), general anesthesia (GA), anterior nasal packing (ANP).*

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Introduction:

Missile injuries of the face, although infrequent in civilian practice, may pose both an immediate threat to the life and may produce delayed complications such as infection and cosmetic problems[1]. The face and neck have many vital structures, which are confined, to small area of the body[1]. This anatomical peculiarity with vital structures like aerodigestive tract, great vessels and nervous system, organs of special senses, any penetrating injury of the region is usually lethal and require thorough examination[1]. The amount of tissue injury and avulsion is directly proportionate to the type of missile causing the injury[2]. There are several factors which plays a role in the destructive nature of a particular missile, the most important of which being the kinetic energy (KE) of the missile[2,3,4], more precisely the dissipation of that KE and tissue density or specific gravity[2,3,4] and also on size of the weapon, the smaller the weapon, the less the damage[5].

Case report:

A 25-year-old male was brought to the emergency department of SMHS hospital Srinagar, (J&K), with the history of missile (bullet) injury of the face. The history also revealed that the patient was shot at a very close range with the handgun and muzzle at a very short distance from the left cheek. There was active bleeding from the both the nostrils and entry side of the wound. The entry wound could be seen over the left cheek, there was no exit wound. The patient was fully conscious, oriented. His vital parameters were stable and was breathing normally through the mouth. Optholmological examination was normal. The neurological status was normal and had no loss of consciousness. On intraoral examination the upper left second premolar was missing. The patient had no systemic problem. The whole face was edematous and black, there was extensive laceration and active bleeding. Anterior nasal packing and pressure packing of the entry wound and lacerated margins was done. I.V fluids (Ringer Lactate) were given. While shifting to the operation theatre the patient was kept in semiprone position. Mean while the radiogram of paranasal sinuses was taken showing the cylindrical foreign body (bullet) in the left maxillary antrum in the vertical position, pointing cranially (Fig 1). It was concluded that bullet entered the left maxillary antrum after piercing the anterolateral wall of the maxilla. Also ABO & Rh blood grouping and cross matching were done. Complete hematological and electrolyte profile was done.

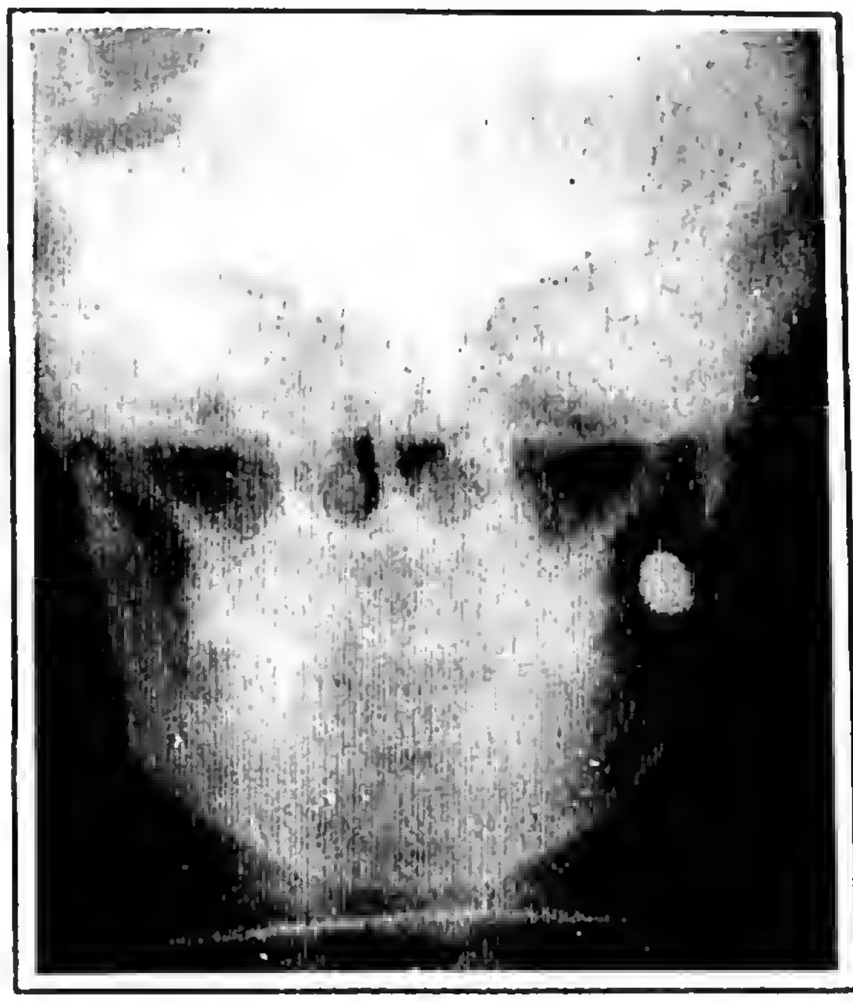

Fig.1: ***A Bullet in the left Maxillary Antrum pointing cranially in near vertical position after being shot by a Hand Gun at point Blank Range on the conteriolateral aspect of the left side of the face.***

Management:

After the initial evaluation and preaneasthetic checkup, the patient was shifted to the operation theatre in the

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semiprone position. UAAP, GA was given through the endotracheal tube; a sublabial incision was given to allow rigid fibro- optic endoscopic visualization of the area from different angles. Then through the canine fossa an opening was made in the anterolateral wall of maxillary sinus for exploration, a bullet in the vertical position pointing cranially was removed with gentle dissection. The wound was irrigated with copious amount of saline and minimally debrided, foreign bodies/material removed and inferomeatal antrostomy was done followed by sinus irrigation the wound was closed. Also the postoperative antibiotics and tetanus prophylaxis were given. The postoperative period was uneventful.

DISCUSSION:

Missile injuries of face, Head and neck may produce anxiety, feeling of futility and therapeutic inertia on the part of the treating surgeon on seeing the patient[5], hence requires well organized and disciplined approach to the care. A missile injury though infrequent in civilian practice is common in Kashmir accounting for second measure cause of maxillofacial injury[7]. Handguns, Pistols are smaller weapons produce less damage[5] due to their lesser kinetic energy[2,3,4,8]. Gun shots from close range, less than three yards i.e., point blank range produces extensive tissue damage referred as blast injury[2,9] and all contents of the missile are found in the wound site and track. The entry wound and surrounding tissue was actively bleeding thus require pressure-dressing[2], similarly A.N.P was done. Measurement of the vital parameters like pulse, blood pressure and respiratory rate is mandatory to look for the life threatening complications like Hypovolumia, shock, and respiratory embracement as the patient may require immediate maintenance of BP and airway management[2,4,5,6,10]. Complete opthalmological examination and neurological status evaluation is necessary due to their close proximity to maxillofacial complex[1,3,5,6,10]. To prevent pooling of blood in natural airways patient should be kept in prone or semiprone position[2]. Skull/facial X-rays are important in determining the extent of injury and initial management and location of bullet[1,3,6,]; similarly role of 3.D CT reconstruction has been very informative[10]. A venipuncture should be accomplished at the earliest possible time and blood drawn for baseline studies, include CBC, Electrolytes, Blood Typing and Crossmatching[2]. Also infusion of ringer lactate should be started at once and maintained until vital signs are stabilized and while blood is being crossmatched[2,5,6]. Endotracheal intubation should be done which facilitates the delivery of GA and also serves or maintains airway during operation though in some cases it is followed by tracheostomy if oral and nasal airways are compromised[2,3,5,6,8]. Fibro-optic endoscopic visualization of sinus should be done to know the damage to the surrounding structures like orbital floor, lateral wall of nose and relation of bullet. Bullet should be removed as it may cause contamination of the sinus[1,2]) or may cause damage to the orbital floor[5] or lateral wall of nose with time due to pressure effects. Sinus irrigation should be done through the antrostomy in order to avoid the contamination of the science[1]. The wound area requires careful debridement and excision of non-viable issue and primary closure at the earliest following inside - out and bottom - up principal and thorough irrigation of the wound with copious amount of normal saline[1-5,8,10]. Because of chances of the contamination prophylactic antibiotic and tetanus toxoid should be given[1,2,4,5,6,8]. The patient should be feeded through Ryles nesogastric tube in the post period[2,5,6,8,10] and also maintains oral cleanliness which also requires betadine gargles. Though in some cases gastrostomy is required[3].

Recommendations:

It is recommended that if the bullet is present in the maxillary antrum it should be removed by careful surgical exploration besides sinus irrigation, thorough wound debridement and prophylactic antibiotics and tetanus toxoid. The immediate consideration should be given to ABC (airway, breathing & circulation). The role of fibro- optic endoscopy cannot be ignored.

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CONGENITAL TOTAL EVERSION OF THE UPPER LIDS

Afroz.A.Khan; A.R.Nasti; Manzoor.Q.Keng; Ayub.M.Dar

Abstract: *Congenital total eversion of upper eyelids is rarely reported in the ophthalmic literature. Lid margins may be everted in microphthalmos and bupthalmos. Some cases have been managed conservatively by injecting hyaluronidase into the chemotic conjunctiva followed by placement of a lid suture to revert the eyelid. This case documents no response to conservative management, but to surgery.*

Key words: *Eversion; Tarsorraphy*

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CASE REPORT:

Twenty days old male baby born by a full term normal delivery presented to the department of ophthalmology Government Medical College, Srinagar with edematous, chemotic and everted upper eyelids, covered with scanty mucoid discharge (Fig. 1). The condition was said to be present since birth. No other external anomaly was noted.It was difficult to examine the globe and the fundii at this stage due to marked chemosis. General physical examination was unrevealing.Three weeks latter when the eyelids reverted to normal position both globes and fundii were found to be normal. Conjunctival swabs and scrapings showed pus cells and staphylococci.

Hot saline packs and antibiotic ointment were applied with injection of hyaluronidase into the chemotic conjunctiva for one week. During this period plastic surgery consultation was sought which revealed no skin deficiency of upper lids. After one week the eyelids were manually reverted under general anaesthesia and two vertical mattress sutures placed over silicon struts in both eyes (Fig. 2).After one week the medial sutures were removed on both sides.Then after another week lateral sutures were also removed (Fig. 3).Thus

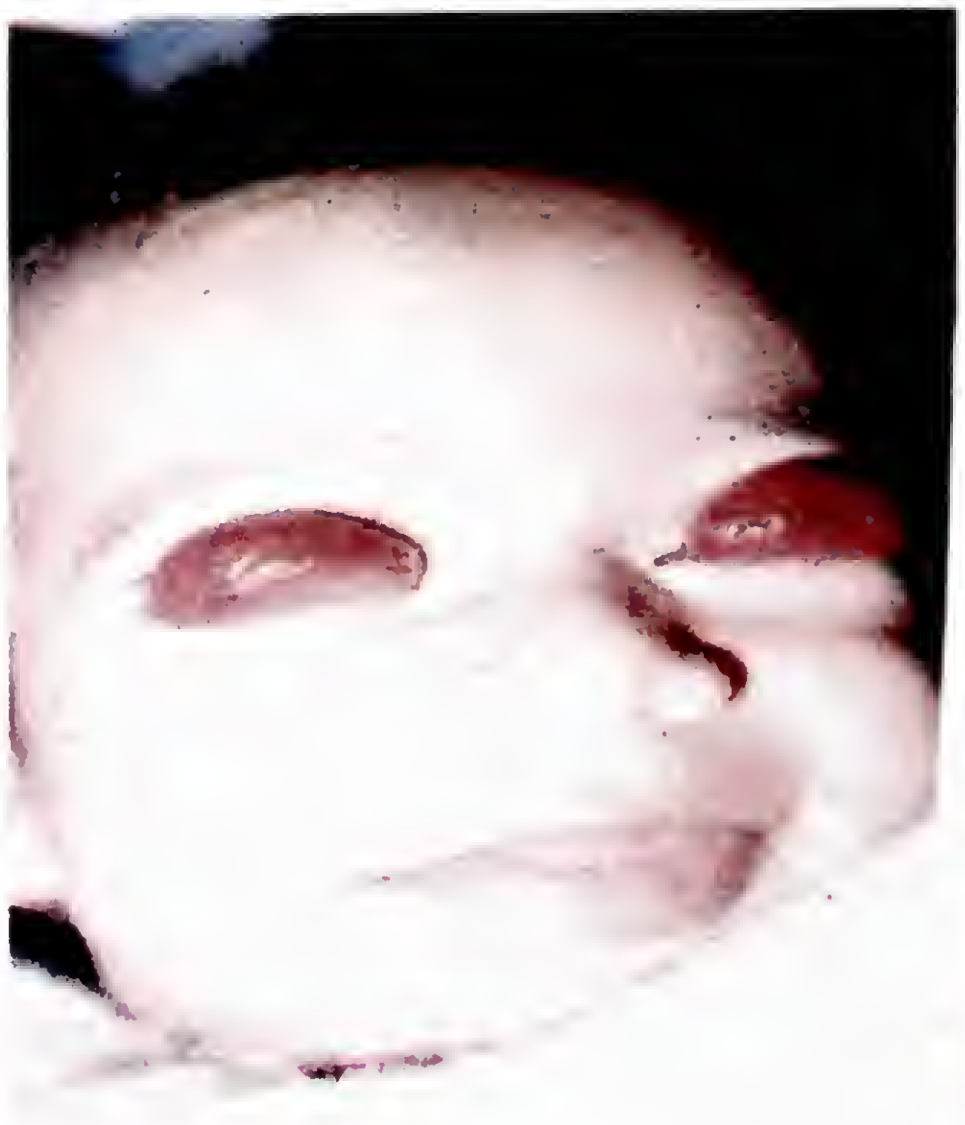

Fig.1: Showing Congenital Total Eversion of upper lid.

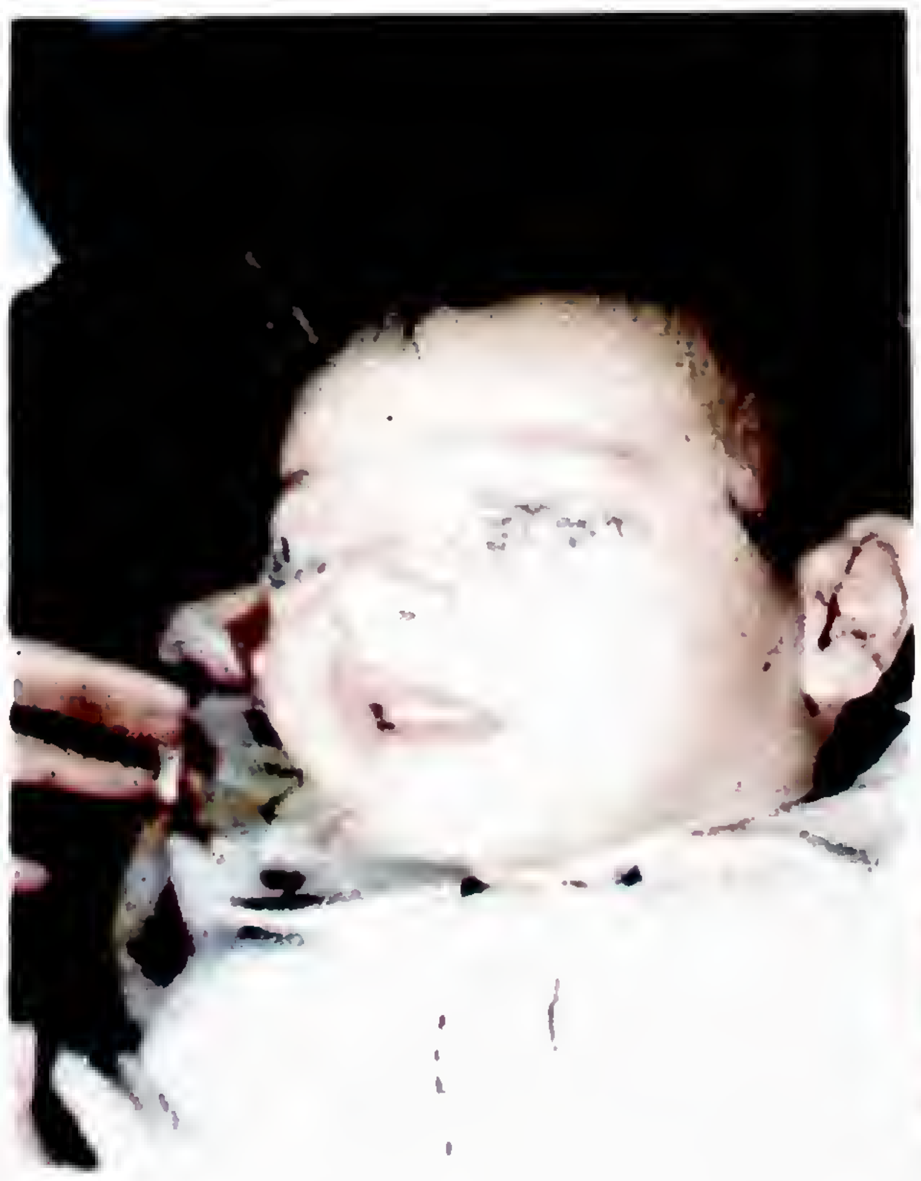

Fig.2: Showing eyelids reverted with tarsoraphy on both sides.

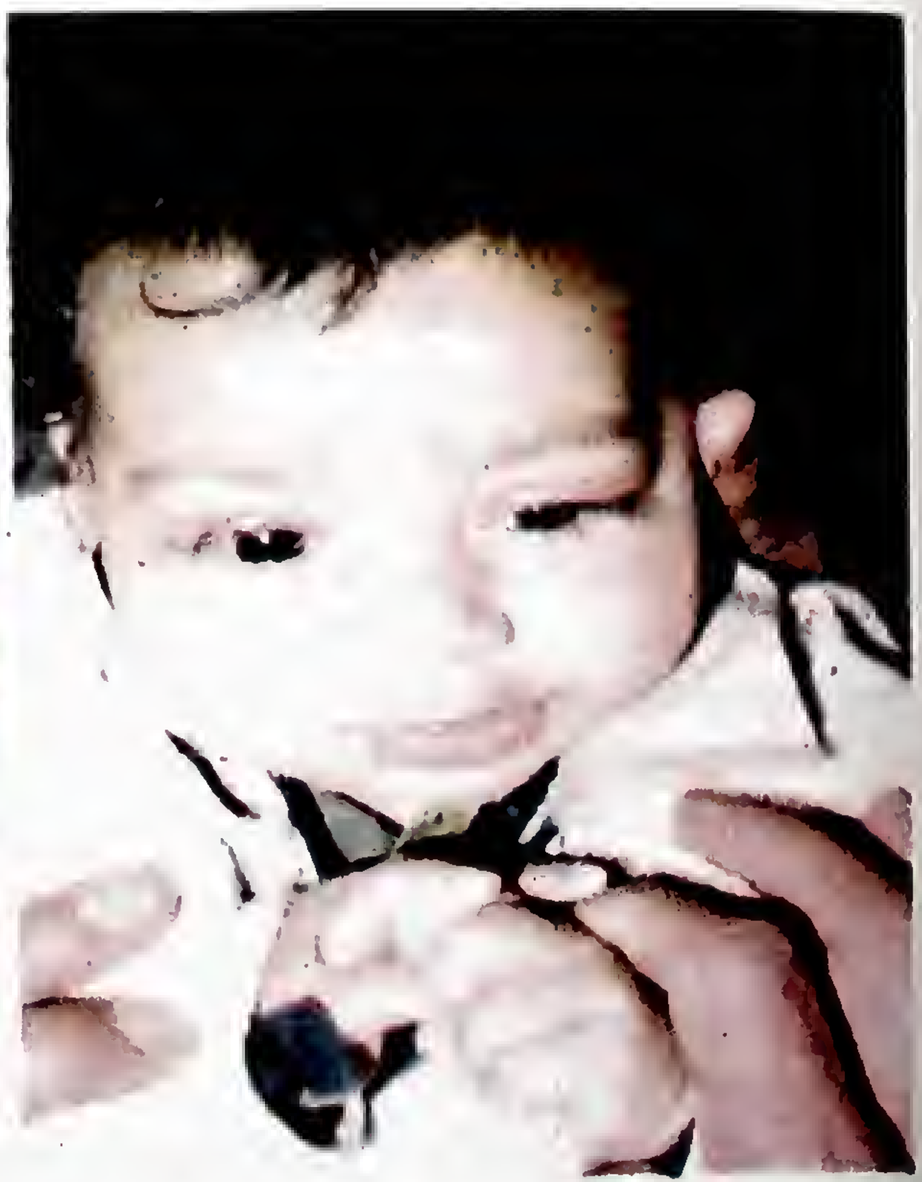

Fig.3: Showing correction of the upper eyelids two weeks after removal of Sutures;

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the baby had an uneventfull recovery within two weeks after surgery.

DISCUSSION:

Congenital eversion of the upper lids is a rare condition [1]. The eversion of upper lids is brought about mechanically as the head traverses the birth canal [2]. Facial trauma against the uterus may also cause interference with the venous drainage in the eye lids and periorbital tissue, resulting in the eversion[3]. Complicated delivery and eyelids defects are reported to contribute to the condition[4]. However in our case these factors did not play a role.

Surgical correction of congenital total eversion of the upper eye lids has been advocated, utilizing various procedures such as hot saline packs with local injection of hyaluronidase,[1,5] tarsorrhaphy [6], skin grafts to upper eye lid [7] In our case patient was managed surgically. Patient responded to this treatment without any ocular damage.

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HEPATOPULMONARY SYNDROME AND PORTOPULMONARY HYPERTENSION

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Cirrhosis affects the function of virtually every organ system in the body. The lungs are no exception. Up to 40-50% of cirrhotic patients report dyspnea upon direct questioning. A similar number are also noted to have abnormal pulmonary functions and arterial blood gases.

There are several mechanisms by which pulmonary dysfunction occurs in cirrhosis. These include mechanisms related to cause, consequence or coexisting pulmonary disorders. Alpha-antitrypsin deficiency, primary biliary cirrhosis (hepatic fibrosis), cystic fibrosis etc. are examples where pulmonary dysfunction is related to mechanisms attributing to liver disease simultaneously. On the other hand tense ascites or hydrothorax can lead to pulmonary problems as a consequence of portal hypertension arising from cirrhosis. However, pulmonary dysfunction in cirrhosis can also be secondary to primary pulmonary disorders e.g hepatopulmonary syndrome and portopulmonary hypertension.

Hepatopulmonary Syndrome (HPS)

Hepatopulmonary Syndrome (HPS) is defined by

- liver dysfunction and portyal hypertension
- Increased alveolar-arterial oxygen gradient
- Abnormal pulmonary arterio-venous communications

Up to 40% of cirrhotic patients meet these criteria. Only 8-10% have impaired oxygenation. Also, only a minority have severe disabling hypoxemia. While it was previously only diagnosed in the absence of hydrothorax, there is no reason why it can not occur even in the presence of hydrothorax.

Pathogenesis

Among the main pathogenetic mechanism believed to be responsible for HPS are abnormal response to increased endothelin-1, increased nitric oxide (NO) production in the liver and abnormal vascular remodeling in cirrhosis. However, no specific etiology has been particulary associated with this condition. It has been reported in the absence of cirrhosis, though, most such cases have portal hypertension e.g Budd Chiari syndrome etc. It has also been reported in acute liver failure but is very rare in this setting.

Clinical Features

The main symptoms of HPS are referable to pulmonary system and include shortness of breath, platypnea, cyanosis, clubbing and spider naevi.

Diagnostic Evaluation

The basic principle is to document the presence of arterial deoxygenation, intrapulmonary vasodilation in the presence of liver disease. The arterial blood gas (ABG) analysis in HPS will reveal impaired arterial oxygenation represented by hypoxemia or increased arterial-alveolar gradient (A-a) of >20mmHg. Once A-a Gradient abnormality is established further investigations may help in diagnosis of HPS. Chest radiography may show hydrothorax but may be normal as well. Pulmonary function tests will mainly help in excluding obstructive or restrictive pulmonary disease. Contrast echocardiography can be used to exclude intracardiac R-L shunts. On this study pulmonary vasodilation is diagnosed by delayed visualization of intravenously injected agitated saline (after 3" heart beat). This is more sensitive than lung perfusion scans. Transesophageal echocardiography is more sensitive than transthoracic echocardiography. Radionuclide lung-perfusion scans are more specific but less sensitive than contrast echocardiography. It allows quantification of the shunt. It is not a screening tool but rather a quantitative instrument. Pulmonary angiogram, though, invasive can reveal either diffuse spongiform pulmonary vessels in arterial phase or small discrete A-V malformations. Natural History

The likelihood of progression of HPS once it develops is not clearly known. The risk factors for its development are also not well understood. In most patients, it does not add to morbidity or mortality. Clinically apparent hypoxemia is however a bad prognostic indicator and is associated with a high mortality. Those with severe hypoxemia have a poorer post-transplant outcome.

Therapy There is no established therapy of HPS. The modalities that have tried include somatostatin, plasma exchange, garlic, Indomethcin, Methylene blue and aspirin, These are mostly anecdotal series. Transjugular

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portosystemic Shunt (TIPS) has been used with varying outcomes. It is not a standard or accepted treatment of HPS. Liver transplant is the only treatment which has shown to improve gas exchange in 85% of subjects. Those with severe gas exchange abnormalities have a poorer outcome after transplant. In those with severe hypoxemia who have a discrete A-V shunt, embolization may bring dramatic relief. Pulmonary angiogram is required to define the presence of these shunts and are performed in those with arterial oxygen of 150mmHg or less on 100% oxygen.

Portopulmonary Hypertension

The porto-pulmonary hypertension is defined by mean pulmonary arterial pressure (MPAP) of >25mmHg and pulmonary capillary Wedge Pressure (PCWP) of < 15mmHg in the setting of portal hypertension. Among the other definitions that have been used include the elevated transpulmonary pressure gradient i.e MPAP-PCWP>10mmHg and increased pulmonary vascular resistance > 120 dynes/sec/cm-5. About 0.73 % cirrhotic patients have histologic evidence of pulmonary hypertension compared to 0.13% of general population. Also, 2% of cirrhotics have increased MPAP on right heart catheterization. It can occur in the presence of portal hypertension even without liver injury. Cirrhosis occurs for 7-8% of all cases of pulmonary hypertension.

Pathogenesis:

The postulated mechanisms for development of portopulmonary hypertension include abnormal production or response to vasoactive substances, endothelial injury and vascular remodeling and a possible role of microthrombi from portal circulation, though, the last one is the least favored hypothesis. Clinical Features

Among the prominent symptoms and signs of portopulmonary symptoms include fatigue, dyspnea, edema, increased jugular venous distensions and tricuspid regurgitation. The danger signs include syncope and chest pain and indicate poor prognosis.

Diagnostic Evaluation

Clinically one can hear accentuated pulmonary component of heart sound which is specific but not sensitive. On the other hand echocardiographic assessment of right heart pressure is specific but not sensitive. Also electrocardiogram shows right ventricular hypertrophy and right bundle branch block which are also specific but not sensitive. Right heart catheterization is the only accurate way to make the diagnosis which is invasive at the same time.

Natural History

Portopulmonary hypertension carries poor prognosis especially when it is severe. When the MPAP is > 35mmHg, post-transplant mortality approaches 50%. Therapy There is no well-proven therapy of portopulmonary hypertension. Pulmonary vasodilators have been used and should be tried with a MPAP >35mmHg. Initially, the acute response to inhaled Nitric Oxide (NO) or intravenous prostacyclin is measured and if a substantial drop occurs, vasodilators e.g prostaglandins etc are used. In two small studies, chronic Prostaglandin infusions were used to keep MPAP down and the patients taken to transplant. It may serve as a bridge to transplant in selected cases. Beta-adrenergic blockers and anticoagulation should not be used in such cases. The patients with MPAP < 35mmHg have no increase in mortality after transplant which should be performed if otherwise indicated. In those with high MPAP, transplant is contraindicated due to high mortality. The natural history of those transplanted (liver) with portopulmonary hypertension is not well defined. The role of multi-organ transplant remains to be better defined.

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FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) OF PARAGANGLIOMAS. A STUDY OF 52 CASES.

A.R.Khan

Abstract: *52 Para -gangliomas were diagnosed on FNA Cytology over 15 year period (1988 – 2003) in more than 40,000 FNA's, conducted personally by the author. There were 46 tumors from head and neck.5 from retro-peritoneum (one presenting as metastasis to sternum), and one from urinary bladder. Head and neck tumors represented high altitude tumors of indigenous patients of Kashmir Valley, with its plains at 1700m above sea level. These included 42 from Carotid bodies, 2 from Tympanic bodies, one from superior cervical ganglion & one from Vagal body. Age of the patients varied between 14 –80 years with 40 females & 6 males. 43 cases were unilateral & one case (CBP) was bilateral, There was no side predilection. CBP, SCP &VBP presented as painless nodule or bulge in the upper neck. TBPs presented as tinnitis & bulge in deep pharynx & small vascular bluish polyp was seen in the ear canal. Duration of nodule/bulge varied between 3 months to 15 years. All the patients showed very gradual increase in swelling & had a benign course. One patient with TBP showed local aggression & infiltration of the overlying brain, killing the host 4 ½ years after the diagnosis. Histopathlogy was available in 29 patients, from excision of tumor in 27 cases (25CBP, 1 SCP,1 VBP) & from incisional biopsy in 2 cases (2TBP) ,which confirmed the FNA cytology diagnosis.. Five cases of retroperitoneal tumors were also aspirated 4 from abdomen presenting as vague mass & discomfort & one from soft tissue mass over sternum representing metastasis from retropirtoneal tumor. There were four males & one female, with age range of 28 to 70 years. Histopathology was available in 4 cases, from incisional biopsies (inoperable malignant tumors)in three cases and from exisional biopsy of one case, which confirmed the FNAC diagnosis in all the four cases. The fifth patient presenting with sternal metastasis in a 70 year male, was lost to follow up. One case of urinary bladder paraganglioma, an 18 year male presenting with mass in lower abdomen accompanied by constipation & hydro-nephrosis was also aspirated & given a clear cut diagnosis of Para-gangliomas. Surgery confirmed a Para-gangliomas (Benign) in bladder wall, All the 52 tumors were non- functional. Aspiration smears were bloody. Basic smear pattern included low moderate to high cellularity with blood in the background. Tumor cells showed round, oval & spindly nuclei, moderate to marked aniso-nucleosis, occasional intra-nuclear cytoplasmic vacuolation, binucleation & giant nuclei with finely granular chromation & moderate pale vacuolated to granular ill-defined cytoplasm. Tumor cells were seen in loose & tight groups, in vagne acini & individually dispressed. Naked nuclei were common. Smear pattern in benign & malignant tumors, primary & metastatic was indistinguishable. Necrosis & mitosis were conspicuous by their absence in all the cases. FNAC diagnosis of Paragangliomas was made in unequivocal language in all the cases without suggestion of any differential. There were no false negative or false positive reports. No complications immade or delayed were recorded in any of the cases. This is the largest study of FNA of head & neck Paragangliomas in the literature & the first report of FNA diagnosed of SCP,VBP,TBP & urinary bladder tumor.*

The study shows that FNAC can be not only quick & but also cheap & reliable in the diagnosis of paraganglioma irrespective of the site. This would help the surgeon to plan the management, without any last minute surprises at the operation table.

Key words: *FNA Cytology (Fine Needle aspiration cytology) CBP- Carotid body Paragangliomas. SCP- Superior cervical Paragangliomas. VBP- Vagal body Paragangliomas. TBP- Tympanic body Paragangliomas. RPP- Retro peritonis Paragangliomas. UBP- Urinary bladder Paragangliomas. Metastatic Paragangliomas.*

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Introduction:

Paragangliomas are the tumors of the chief cells of the paraganglia derived from the neural crest [1].Paraganglia are widely distributed in the body with some specific localisations in the head & neck & retroperitonum. At low altitudes 80-90% paragangloimas arise in the adrenal medulla & a small proportion in the extra-adrenal locations mostly at Para-aortic & Para- vertebral sites[2,3] .In the head

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& neck these tumors are rare at low altitudes & but have higher incidence at high altitudes[4,5].Further these tumors at low &high altitudes differ in a number of ways. Low altitudes may be sporadic (90%) or autosomal dominant (10 %) and are seen at a median age of 50 , without gender predilection.37% of familial tumors are bilateral compared to 5% in sporadic tumors[5,6].The high altitude tumors are very slow growing, seen over a wide age range, show very high female predilection &,are non functional, unilateral & benign in behaviour[5] . The nature of the high altitude tumors is considered as hyperplasia by some[7, 8] & true tumors by others [9,10.] The argument in favour of the neoplastic nature given by the latter authors is the presence of residual normal paraganlion tissue outside the tumor capsule. DNA aneuploidy studies are not available with these tumors unlike low altitude tumors. The incidence of malignancy in paraganglimas is reported to be 6 – 23%[10].This is not applicable to high altitude head & neck tumors. Other frequent site of paraganglimas is the retroperitoneum. The malignancy in Paragangliomas is determinated by lymphnode & distant metastasis as in other endocrine tumors. It is relevant to mention that late recurrence & metastasis after many years after the surgical excision is feature of low altitude head & neck & retroperitional tumors [11-14].

Para gangliomas are diagnosed customarily by selective angiography, CT, MRI & radionuclide scanning. Conley[15] was the first to advocate use of FNAC in the pre-operative diagnosis of Carotid body Paragangliomas. Since then a limited number of reports have appeared in the literature, mainly from the head & neck tumors but a few from retroperitoneal region as well[16-34]. This report is based on author's experience of FNA diagnosis of 52 paraganglimas, over a period of more than 15 years in more than 40,000 aspirations conducted personally by the author.

Materiel & Methods:

Review of records over a period of 15 years. (1988 – 2003) revealed 52 cases of Paragangliomas diagnosed on FNAC. All the FNA were conducted as out-patient procedure. Patients were placed in supine position. In head & neck tumors, the neck was extended & gentle suction applied using 10-20ml disposable plastic syringes with & without syringe holder & 22-24 G disposable needles. In case of retroperitoneal tumors help of USG/CT was taken to aspirate the tumors, using 22G long disposable needles. The bladder & sternal tumors were aspirated directly .All the aspirations were bloody. The material was quickly ejected on 6-10 slides, excess blood sucked with cotton swabs &, 5-6 smears were stained with MGG, 1-2 with heamatoxylin & eosin & 2 - 3 slides were left unstained fixed in alcohol. Adequate diagnostic material was obtained in first attempt in all but 3 cases (cases 9,21& 46). Two of these cases were successfully aspirated in second attempt, whereas the third case yielded diagnostic material on third attempt. During follow up, 5 patients (case 2,10,15,16 & 17) who refused surgery were reaspirated on the request of the physician. The case 2 was reaspirated in 1994, 1997, & 1999.The tumor in this case a nodule less than 2 cms in 1991 grew to a huge bulge (>8cms) in 1999. Case 10 was reaspirated in 1995 & 1997,Case 15 in 2001,case 16 in 1999 & case 17 in 1997.The smears in the repeat aspiration did not show any significant difference in morphology, compared to initial smears. No complications immediate or remote were recorded in any of the cases.

Results:

The clinical data of 52 cases of paraganglioma diagnosed on FNAC is given in table. There were 46 cases from head & neck region, 5 from retro-peritoneum & 1 from urinary bladder. 46 cases from head & neck comprised of 42 CBP, 2TBP, 1SCSP & 1 VBP. Age of the patients varied between 14 & 80 years with 40 females & 6 males. Only one patient (case 45) had bilateral CBP. CBP, SCSP & VBP presented with painless swelling in the upper neck of 3 months to 15 years duration (Figs 1 – 4).On examination the swelling mimicked lymphadenopathy or soft tissue mass. TBP presented with tinnits & deep pharyngeal bulge of several months' duration & bluish small blue polyp was seen in the ear canal. 27 tumors (25 CBP, 1 SCP & 1 VBP) were excised without sacrificing the Carotid vessels indicating compressive nature of growth (Fig.5). In 2 TBP only incisional biopsies were taken. Histopathology confirmed Paragangliomas in all the cases. 45 cases persued a benign course clinically. One patient of TBP, a 40 year female (case 23) showed local aggression by invasion of overlying brain & death 4 ½ years after the diagnosis. Of 5 RPP, with age range of 28 – 70 years, there were 4 males & 1 female. 4 of these tumors presented with mass & discomfort in the abdomen. The fifth patient a 70-year-old male (case 49) presented with a soft tissue mass over sternum with involvement of underlying bone (Fig. 6). FNA diagnosis of Paragangliomas lead to discovery of tumor above left supra- renal in the retroperitoneum (Fig. 6 A). This patient was lost to follow up subsequently. The other 4 patients were subjected to surgery which revealed inoperable tumors in 3 cases (cases 3,24.26) where only incisional biopsies were taken & tumor excised in one case (case 48 fig. 6). The Histopathology confirmed the diagnosis of Paragangliomas, in all the 4 cases. One patient of urinary Bladder tumor (Case 25) a 18-year male was aspirated & was diagnosed as paraganglioma in unequivocal language. Subsequent surgery at TMH Mumbai confirmed paraganglioma (benign) bladder wall.

Cytological Findings:

The smears showed low, moderate to high cellularity

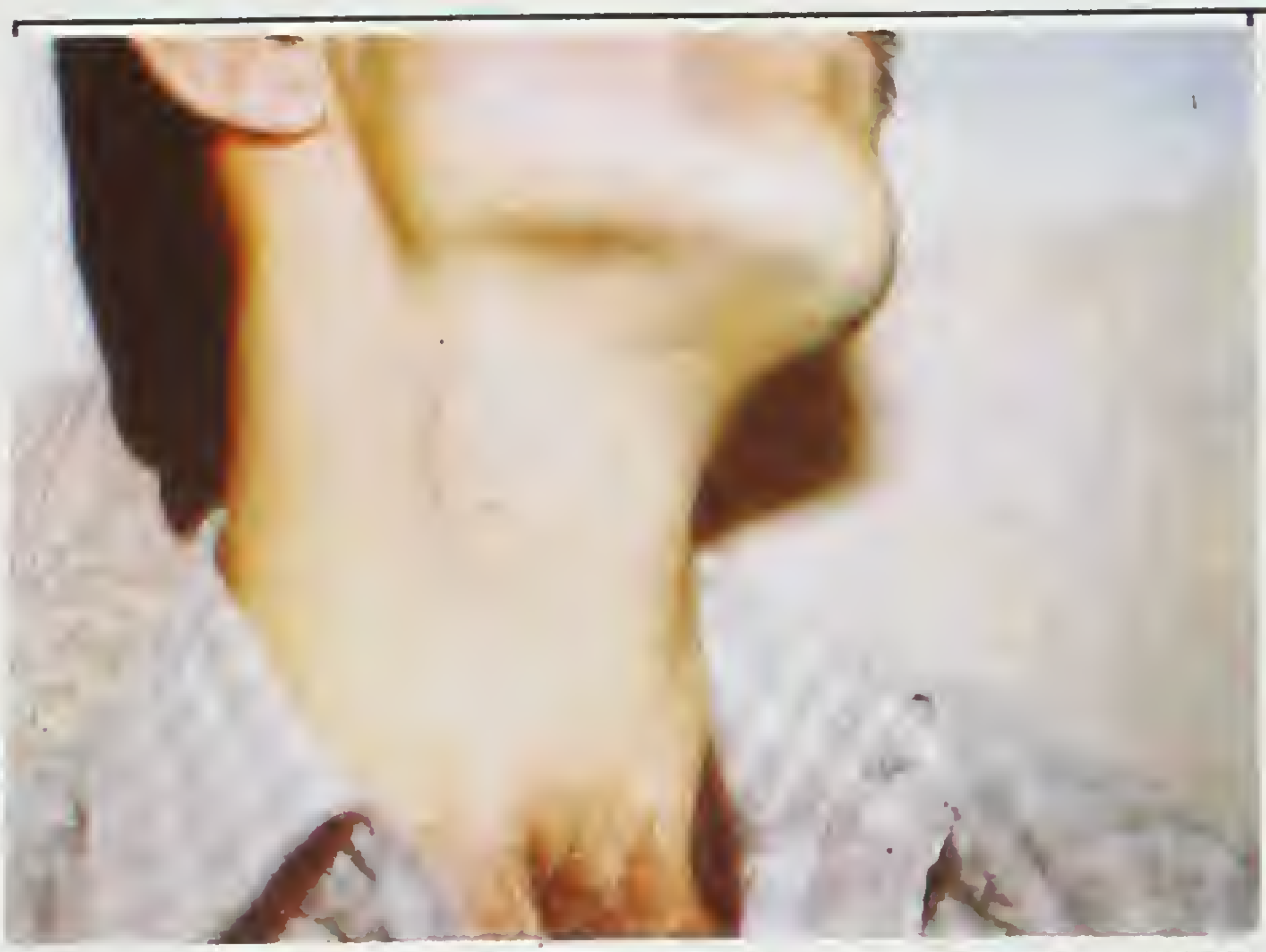


Fig. 1. Shows right Carotid body tumor, barely visible but palpable & encircled by ink.

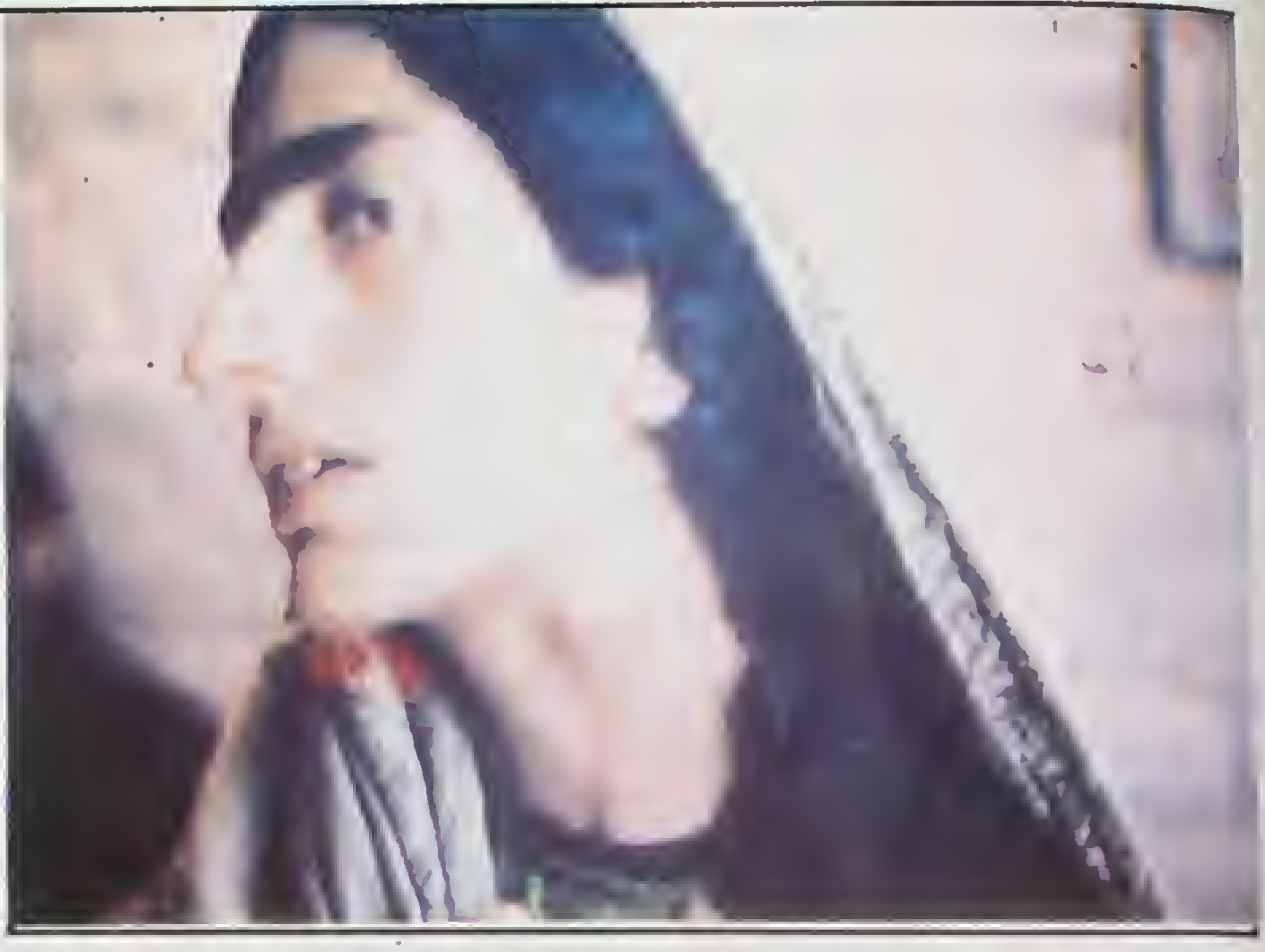


Fig. 2. Left Carotid body tumor, seen as just a visible nodule below angle of left mandible.

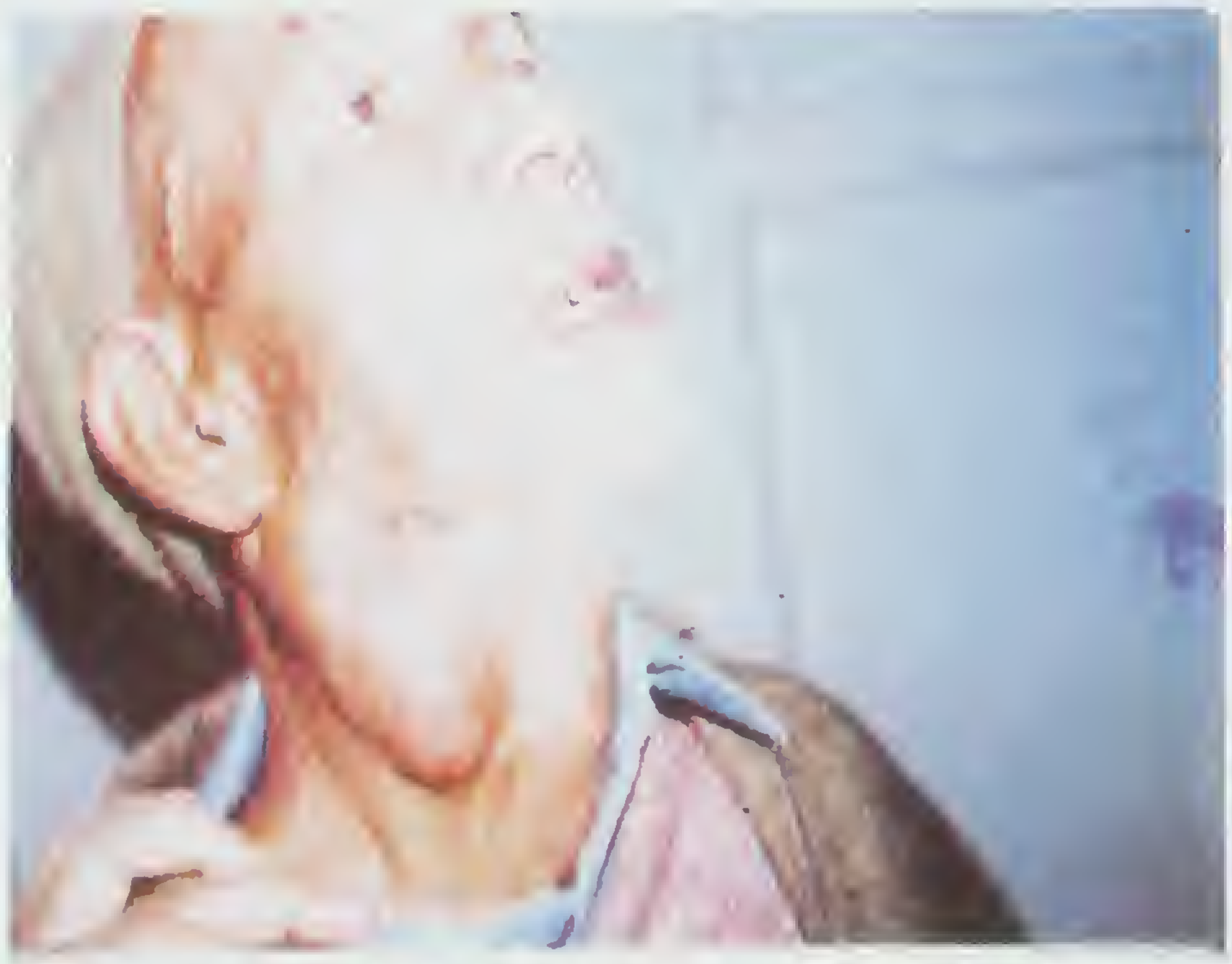


Fig. 3. Right Carotid body tumor of 4 cms diameter.

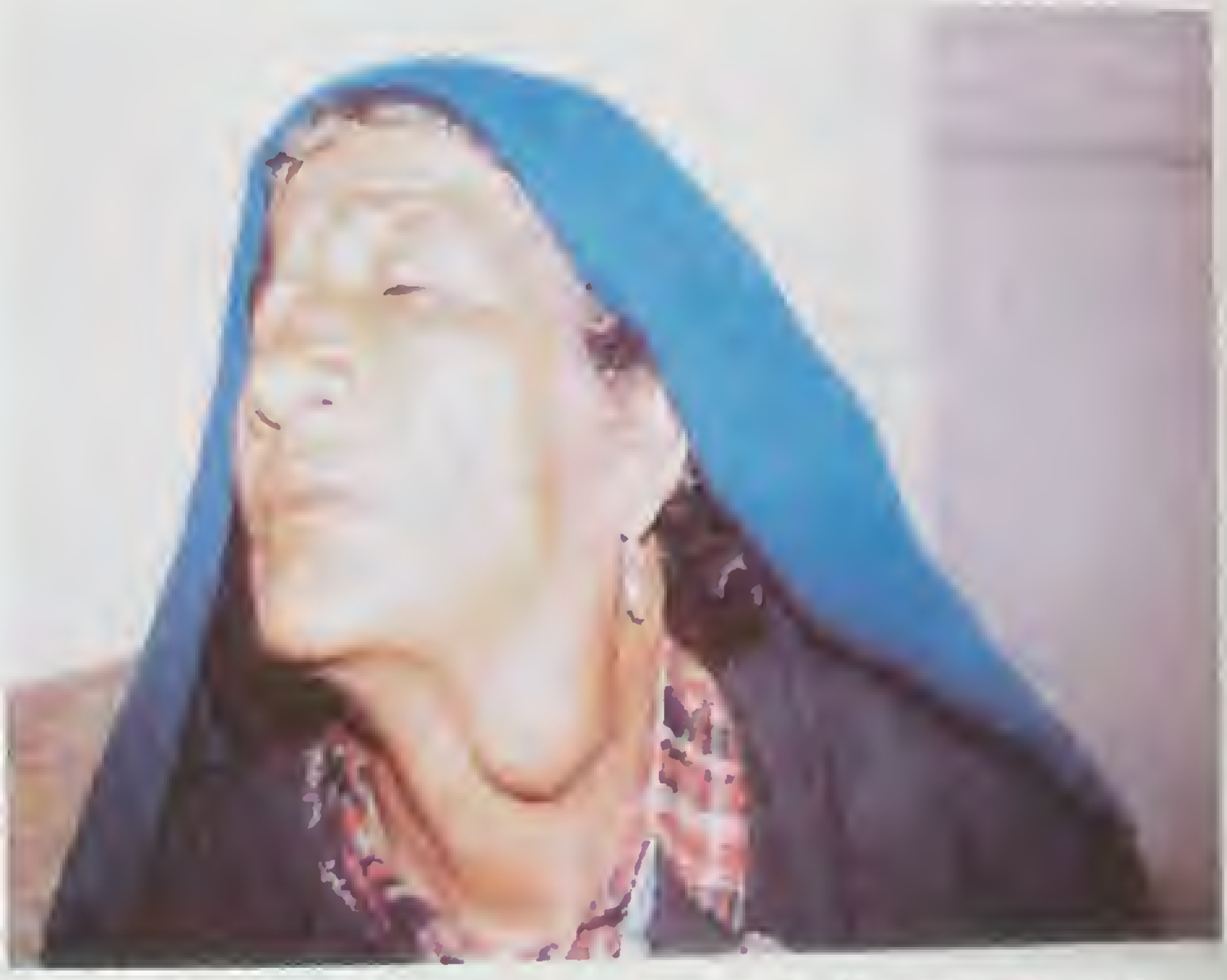


Fig. 4. Left Carotid body tumor > 3 cms diameter.

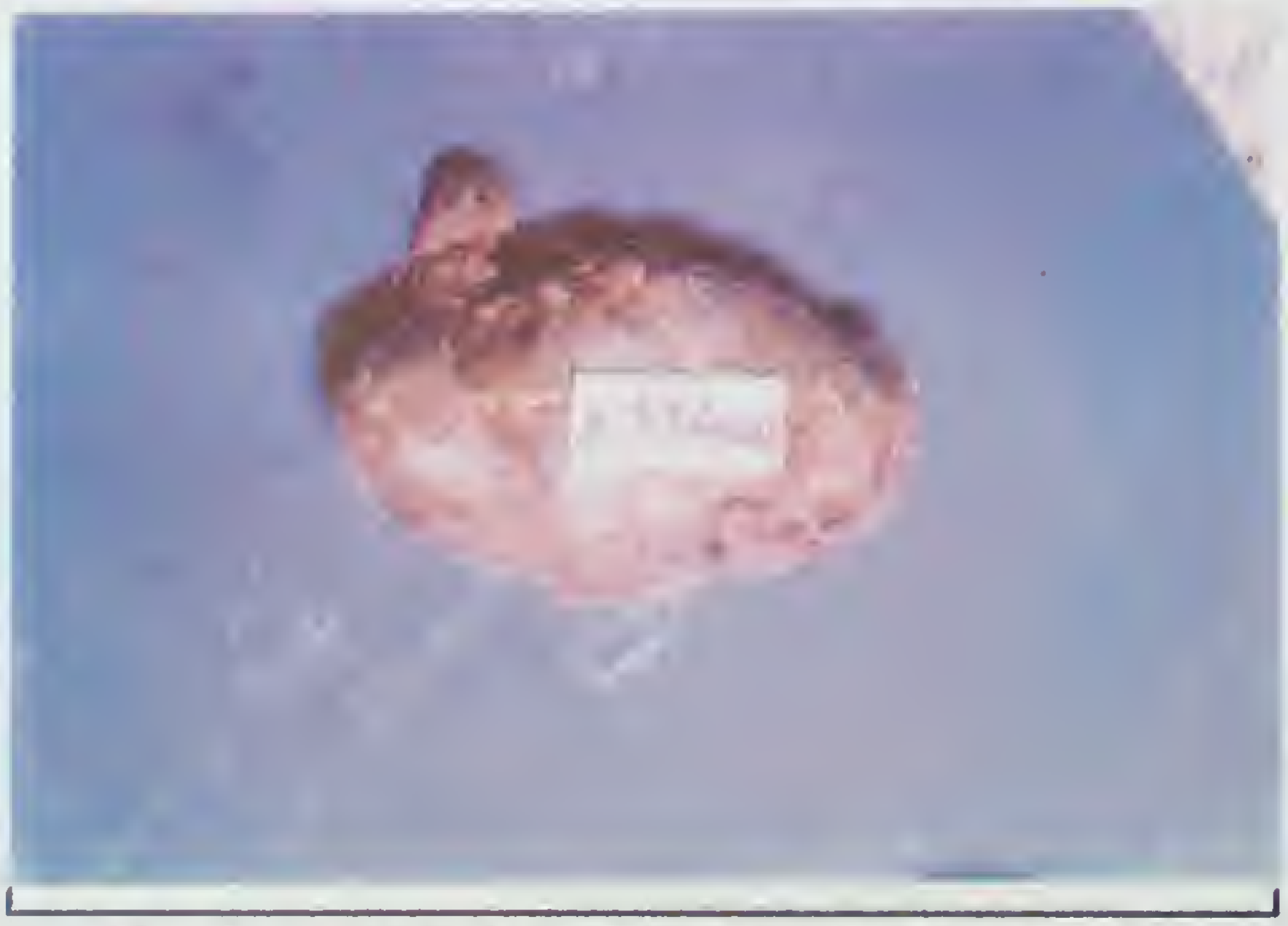


Fig. 5. Gross specimen of a right sympathetic ganglion tumor in a 14-year-old female.

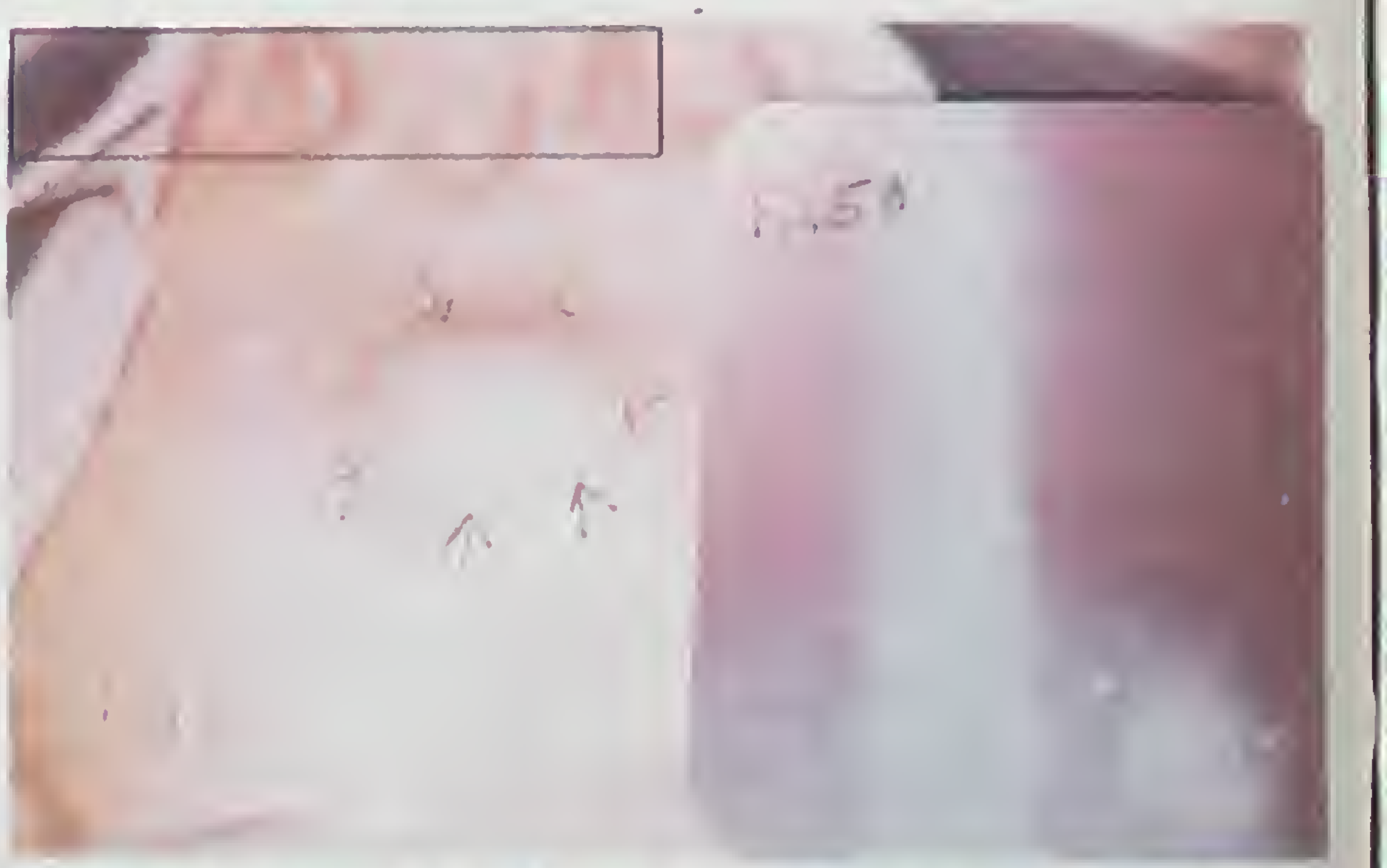


Fig. 6. Shows a soft tissue swelling over sternum (within arrow) of FNAC seen in fig.12.inset

Fig.6A. Plain X Ray abdomen shows a tumor in the retroperitoneium above the left Supra-renal.

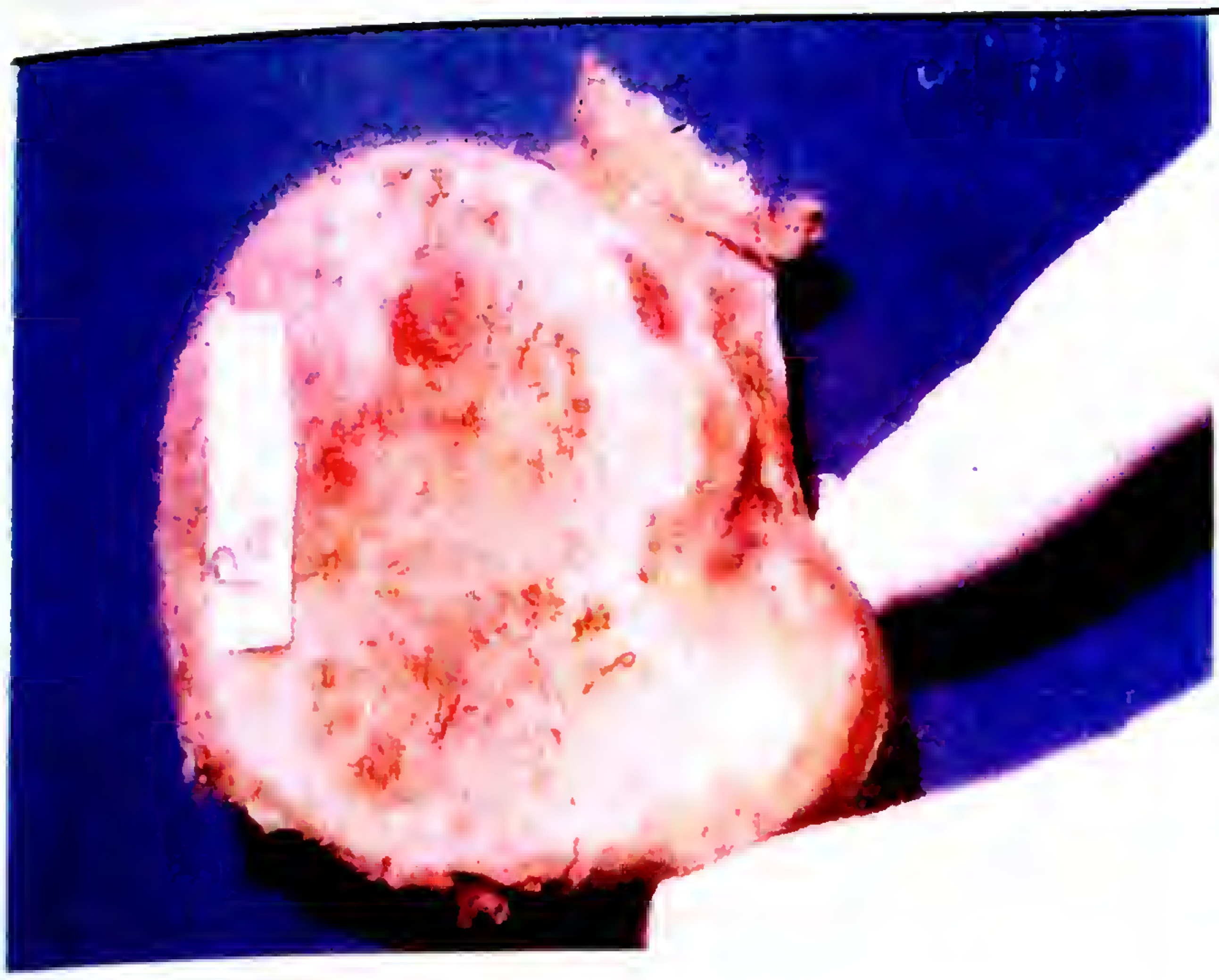


Fig. 7 C/S of retroperitoneal tumor, wellcapsulated > 6 cms diameter tumor. Benign at the time of surgery (case 48).

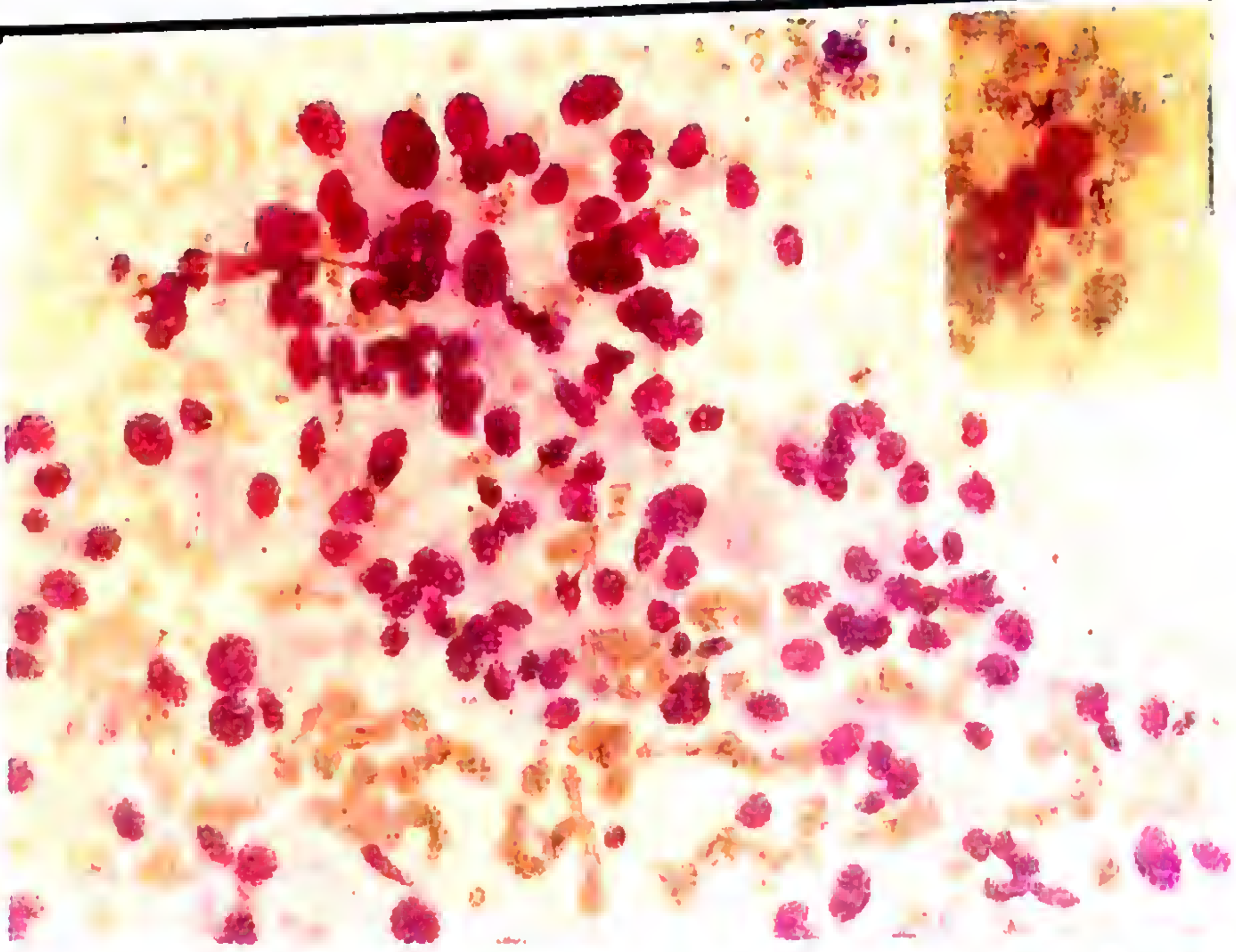


Fig. 8. Carotid body tumor: shows round & oval & spindle cells with moderate aniso-nucleos, & delicate pale ill defined cytoplasm, in loose clusters & dispersed.Inset – cluster of tumor cells, with

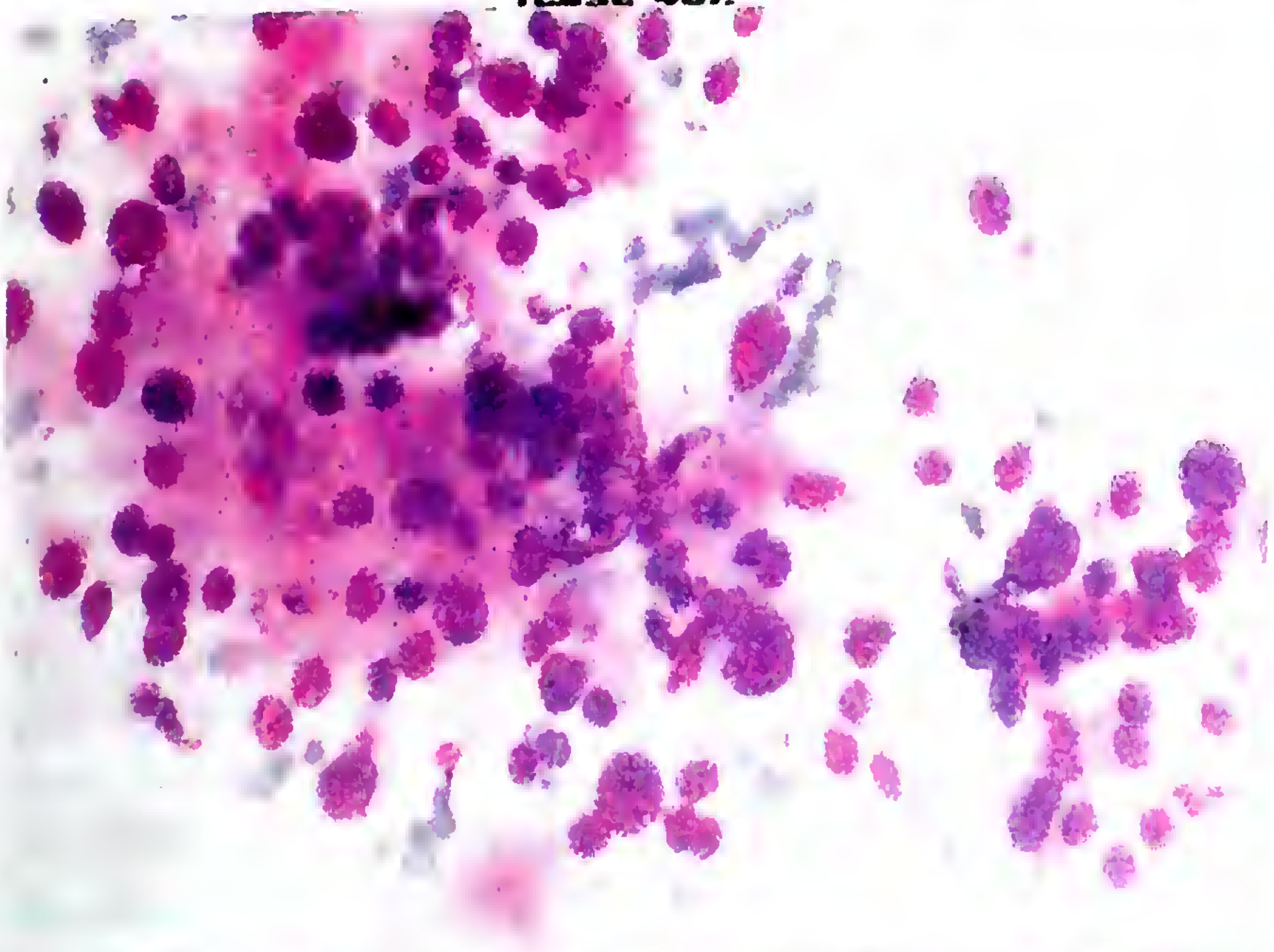
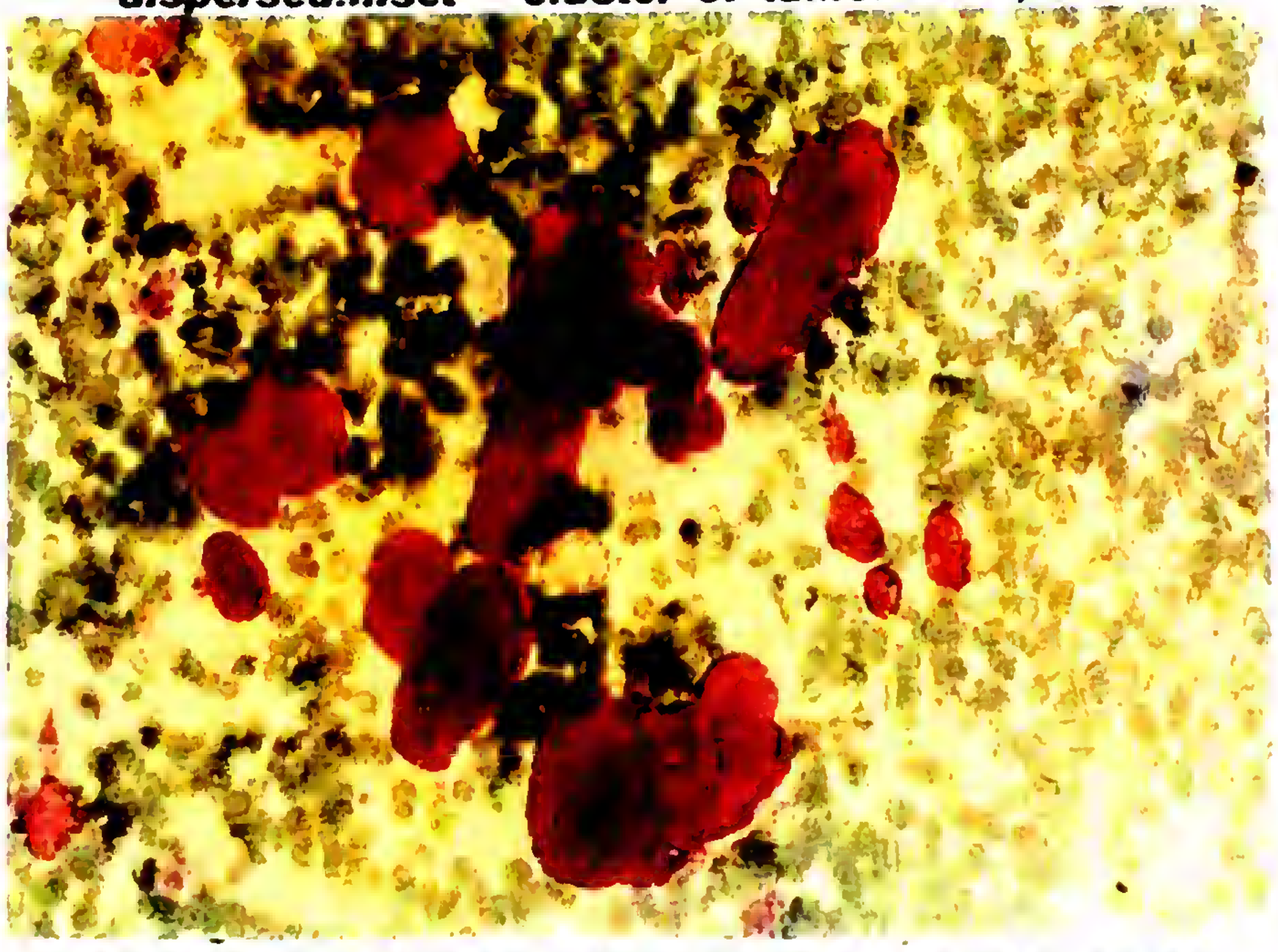


Fig. 9. Retroperitoneal paraganglioma (case 48) with considerable aniso-nucleosis of tumor cells.



paraganglioma-malignant, shows marked aniso nucleies, with gaint nuclei MGGX400.

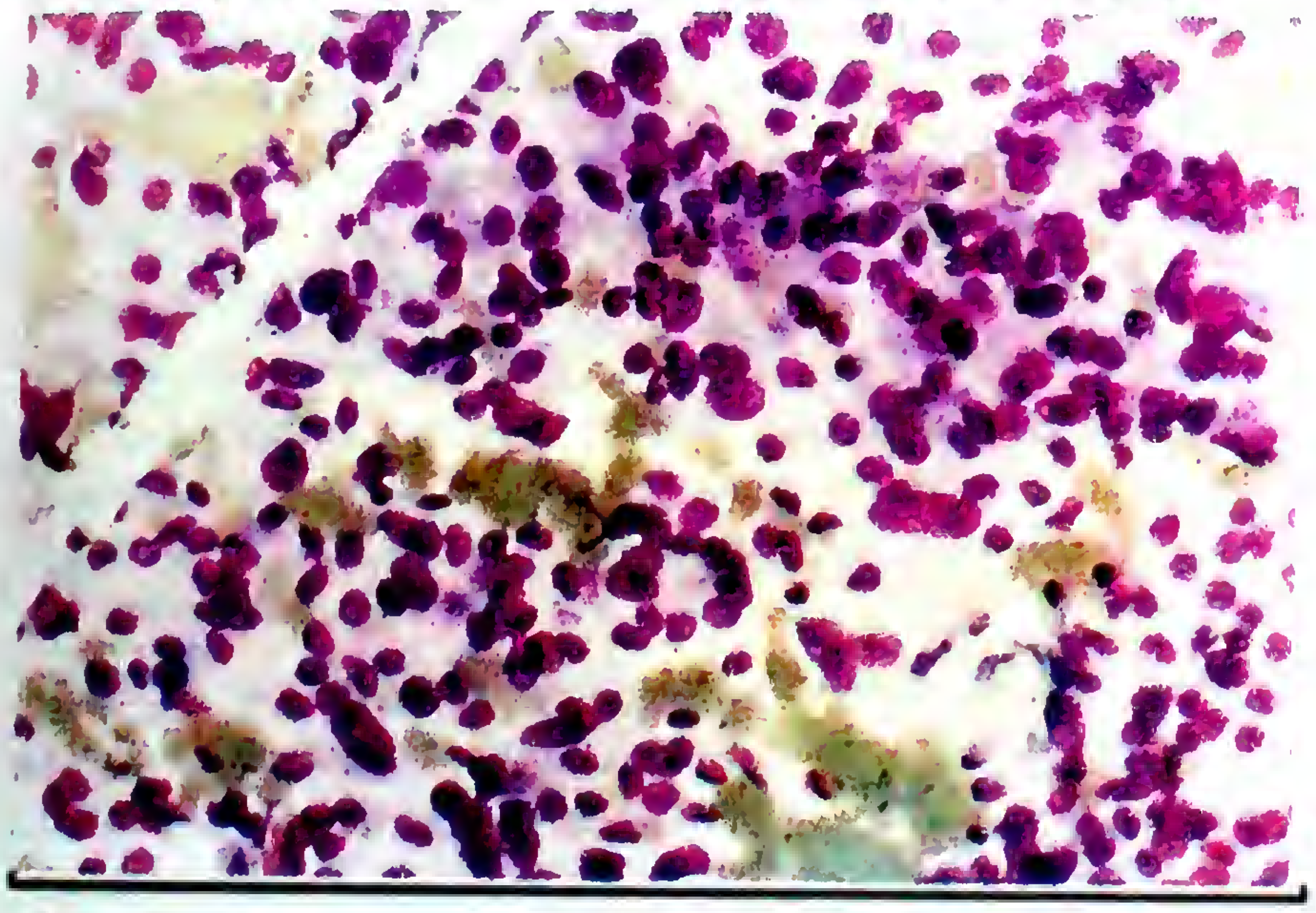


Fig.11. FNAC Urinary bladder Paragangliomas in a 18 year old male, Highly cellular tumor with striking aniso-nucleosis & focal tubular arrangement MGGX400.

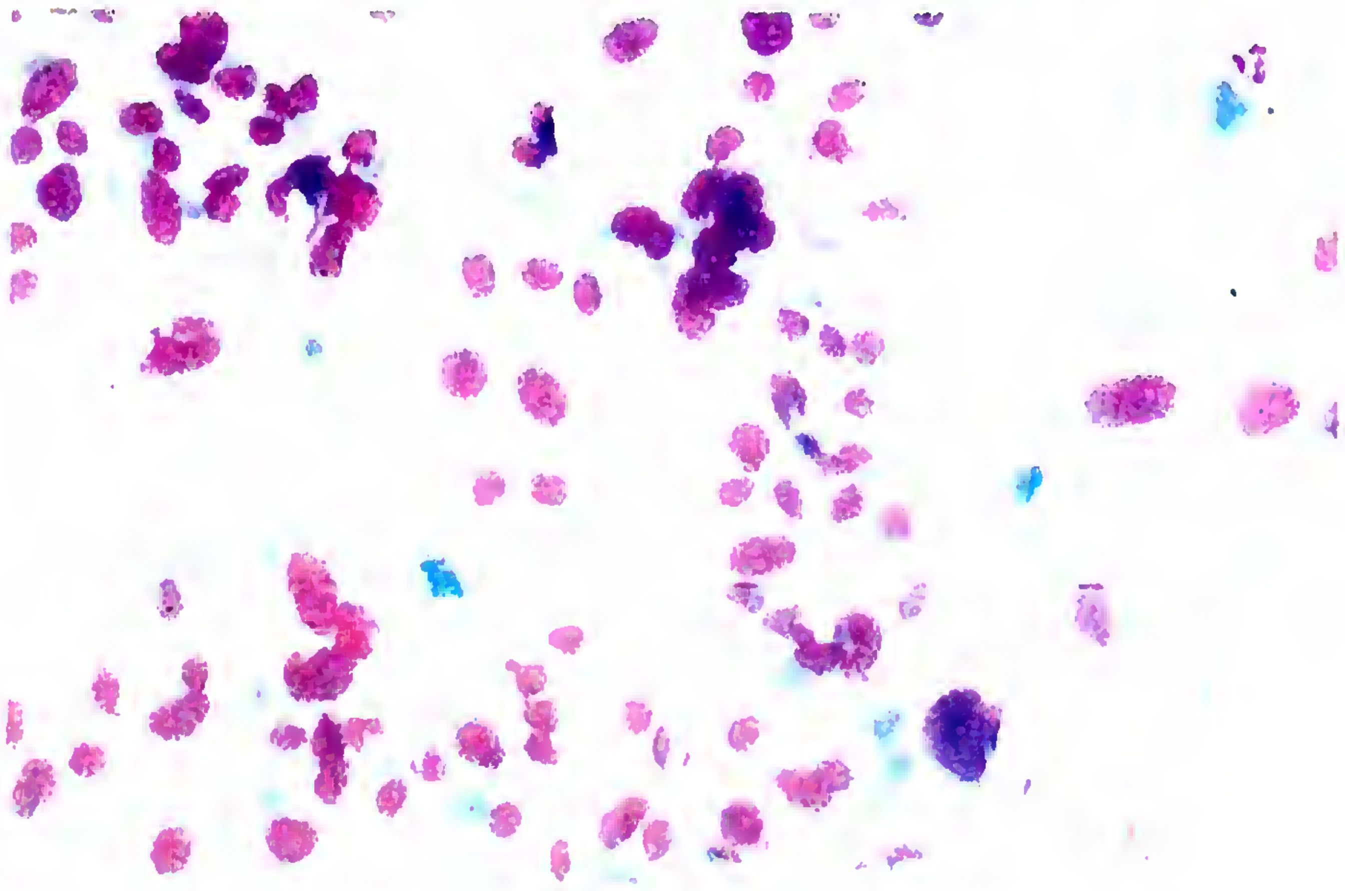


Fig.12. FNAC Metastatic Para-ganglioma from sternum shows considerable aniso-nucleosis of tumor cells MGGX400.

Tumor cells were seen in small & large loose & tight clusters as well as individually dispersed. The nuclei were round to oval & occasionally spindly with finely granular chromatin, with slight to severe anisocytosis & aninucleosis. The cytoplasm was ill-defined pale to vacuolated & granular. A vague follicular arrangement was also seen occasionally. Naked nuclei were common. There were occasional intra-nuclear vacuolations. The background was bloodly. With Carotid body Paragangliomas as prototype, the smears from tympanic body, superior cervical sympathetin ganglion & vagal body were identical. Tumors from retroperitoneal, urinary bladder & metastatic tumor to sternum differed little from the prototype. However some retroperitoneal tumors showed striking nuclear pleomorphism (Figs.8-12).

Table: *FNAC- Paragangliomas (1988 – 2003)*

S.No.	Year	Age/Sex	Anat.Site
1.	1988	50/M	RCB
2.	1991	58/F	LCB
3.	1992	40/M	RP
4.	1993	45/M	LCB
5.	1993	46/F	LCB
6.	1994	55/F	RCB
7.	1994	30/F	LCB
8.	1994	48/F	RCB
9.	1994	68/F	LCB
10.	1994	40/F	RCB
11.	1995	50/F	RCB
12.	1996	35/F	RCB
13.	1996	60/F	RCB
14.	1996	45/M	LCB
15.	1997	41/F	RCB
16.	1997	49/M	LCB
17.	1997	50/F	RCB
18.	1997	60/F	RCB
19.	1998	15/F	RTB
20.	1998	35/F	RCB
21.	1998	50/F	RCB
22.	1998	32/F	LCB
23.	1998	40/F	LTB
24.	1998	35/M	RP
25.	1999	18/M	UB
26.	1999	38/M	RP
27.	2000	25/F	LCB
28.	2000	75/F	LCB
29.	2001	65/F	LCB
30.	2001	58/F	LCB
31.	2001	50/F	LCB
32.	2001	80/F	RCB
33.	2001	72/M	LCB
34.	2001	60/F	RCB
35.	2001	50/F	RCB
36.	2001	60/F	RCB
37.	2001	45/F	RCB
38.	2002	14/F	RSCP
39.	2002	55/F	LCB
40.	2002	35/F	LCB
41.	2002	42/F	LCB
42.	2002	40/F	LCB
43.	2002	50/F	RCB
44.	2002	50/F	RCB
45.	2002	75/M	LCB/RCB(Bilateral)
46.	2002	35/F	LCB
47.	2002	50/M	RCB
48.	2002	28/F	RP
49.	2002	70/M	Swelling Sternum (Metastasis)
50.	2003	24/F	RVB
51.	2003	42/M	LCB
52.	2003	60/F	CBP

Abbreviations:

CB - Carotid body
RP - Retro-peritoneal
SCG - Supeier cervical ganglion
R - Right
UB - Urinary bladder
TB - Tympanic body
VB - Vagal body
L - Left

Discussion:

Conley[15] was the first to advocate the utility of FNAC in the pre-operative diagnosis of Carotid body tumors. Several publications that subsequently appeared mostly favoured [17-29] the procedure & a few opposed it, because of poor yield of malarial in hemorrhagic smears[5] or fear of complications[16]. The most reports of FNAC on Paragangliomas are reported from Carotid body tumors[15-29] with an overall pre-operative false negative as high as 43 %.[6] The largest study of 13 cases is based on retrospective analysis of one study[16], where only 7 cases were correctly diagnosed & authors recommended abandoning the procedure. These authors however have given an excellent smear description of these tumors. Poor results on FNA diagnosis in literature reflect rarity of these tumors at low altitudes[4] & therefore poor encounter & experience of cytopathlogists. The position is different at high altitudes with the higher incidence[5], which is revealed by this study. Authors have also diagnosed 12 tumors from head & neck not preceded by FNA over this period. The Carotid bodies & related paraganglia have a chemosensitive role[35]. Carotid bodies are the largest of the paraganglia measuring 0.5x0.3x0.2cms[36] & weighing about 12 mg at low altitudes. At high altitudes, the carotid bodies are larger than these, because of chronic anoxemia. The presumptive sequence of events would be chronic anoxemia-hypertrophy, hyperplasia & neoplasia of chief cells.

FNAC retroperitoneal tumors are reported infrequently in the literature[30-34]. Five tumors were diagnosed on FNA by the authors, one of which was diagnosed from sternal metastasis which lead to the discovery of primary tumor in the retro-peritoneum above the left supra renal. This patient was lost to follow up subsequently. The FNA diagnosis in other four patients was confirmed on Histopathology from incisional biopsies, in there inoperable

(Malignant) tumors (cases 3,24 & 26) & excision of tumor (Benign, case 49). Retroperitoneal extra- adrenal Paragangliomas represent 10-20% of tumors in this region[2], most originating in the organ of Zucker Kandl & present as abdominal mass & pain (65%), metastasis (10%) or asymptomatic (20%), [38] Only 25-60% are functioning[38]. The tumor are seen in the age group of 30-45 years, with no gender predilection generally & 20-40% behaving aggressinely[38, 39]. Four tumors in the present study were malignant & one tumor was benign at the time of surgery, which needs long follow up because of late recurrence & metastasis of these tumors[13].All the five tumors were non - functioning clinically.

The present case of urinary bladder Paragangliomas diagnosed on FNAC & confirmed by hitopathology (Benign paraglioma) in the bladder wall subsequently is the first case of its kind in literature. Urinary bladder paraganglioma is rarely reported & present with hypertension in 2/3rd, hematuria in ½ the cases, & local aggression in 10%. , though metastasis is rare.[39]

With experience on FNAC of 52 paraglangliomas in this study, the basic smear pattern was same in primary & metastatic sites. However some retroperitoneal tumors showed more striking aniso-nucleosis & giant nuclei (Fig 10) .A lot of differential diagnosis has been mentioned in the literature[16, 24] in FNAC smears. Author is of the opinion that key to the diagnosis is yield of the material in aspirations & it's spread on the slides. Smears pattern is characteristic to leave anything for differential diagnosis. However problems lies in the rarity of Head & neck Paragangliomas at low altitudes & poor exploitation by cytopathologist at high altitudes.

In conclusion, the author feels that cytopathologist has an important role in the pre-operative diagnosis of these highly vascular tumors irrespective of the site. This can put the surgeon at a great advantage to plan the management of these tumors without last minute surprises on the operation table.

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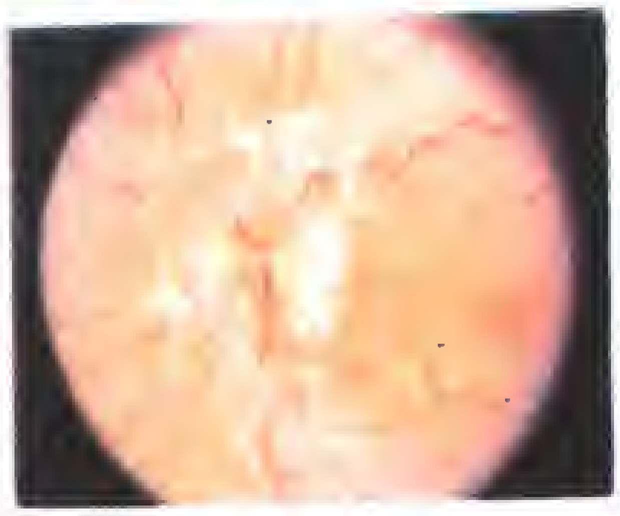
EYE IN HEMATOLOGY (PART II)

Manzoor Qadir Keng, MS; A. R. Nasti MS; M.I. Qadri Ph.D

Plasma Cell Dyscrasias

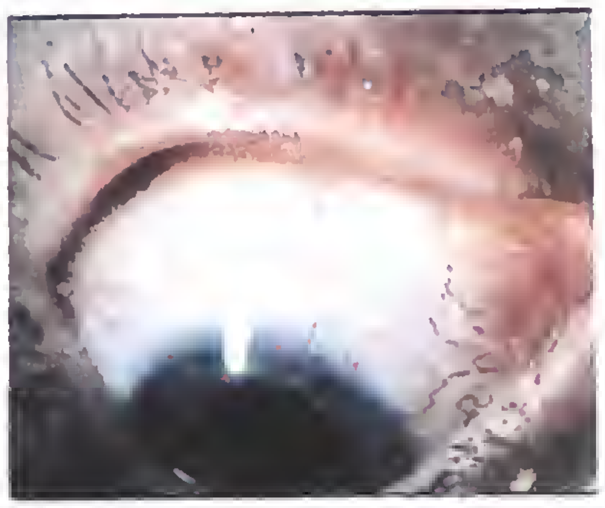
Multiple Myeloma

- Crystals in the conjunctiva.
- Crystals in the corneal stroma.
- Crystals in iris and ciliary epithelium.
- Retinal microaneurysm
- Nerve fiber layer hemorrhages and infarcts.
- Exudative retinal detachment.
- Papilledema.
- Proptosis.
- Choriodal folds.
- Cranial nerve palsies.



Waldenstroms Macroglobulinemia

- Sludging of blood flow in conjunctival vessels.
- Retinal vascular occlusions.
- Exudative retinal detachment.
- Papilledema.

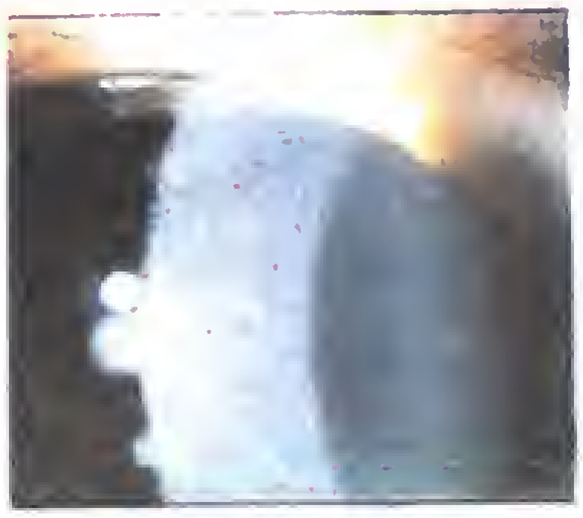


Light Chain Diseases

- Retinal Vasculopathy with capillary nonperfusion.
- Neovascularization.
- Vitreous hemorrhage.

Congenital / Acquired Coagulation Factor Deficiency

- Periocular hemorrhage.
- Pupillary abnormalities.
- Vitreous hemorrhage.
- Retinal hemorrhage.
- Papilledema.
- Cranial nerve palsies.



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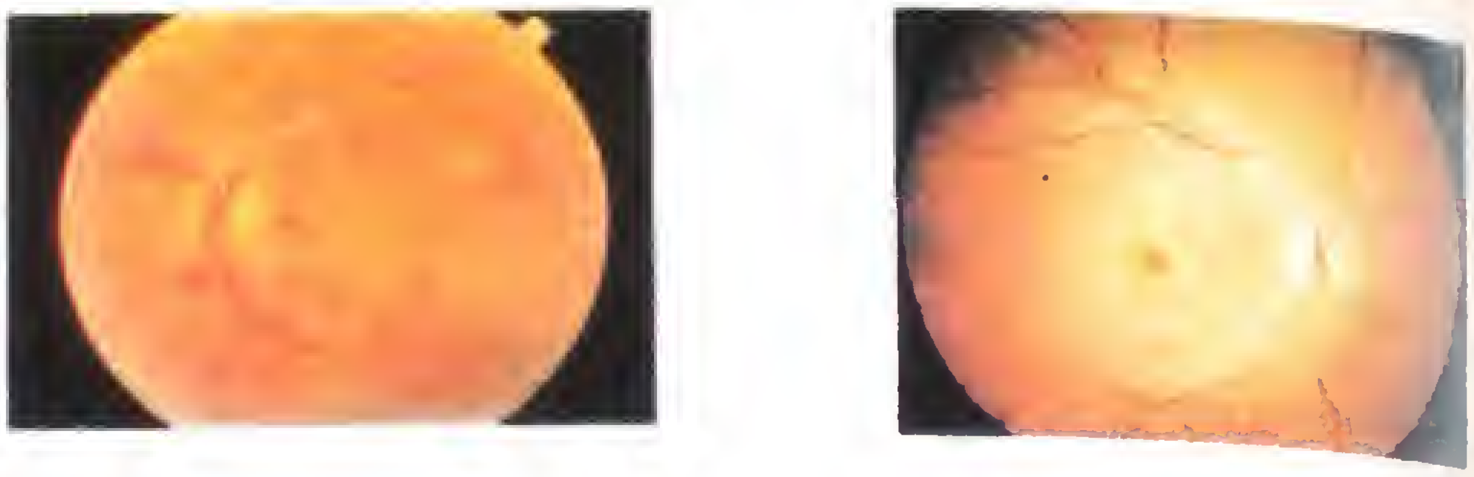
Hypercoagulable States

Antiphospholipid Antibody Syndrome

- Retinal venous and arterial occulusion.
- Neovascularization.
- Vitreous hemorrhage.
- Visual field loss.



Hypercoagulable States

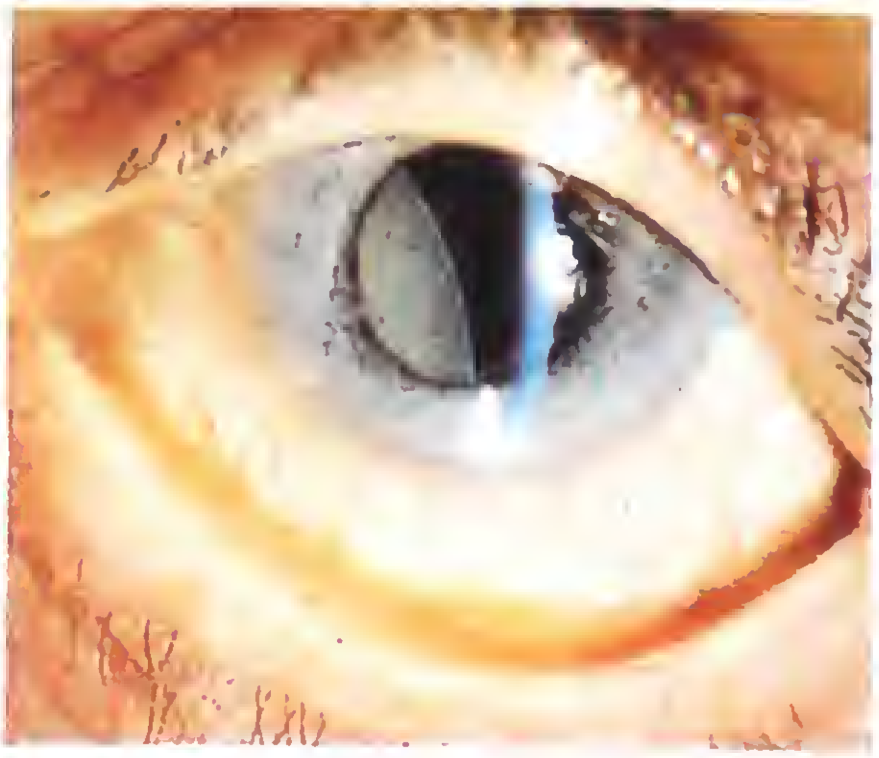
Deficient Natural Anticoagulants.

Protein C and Protein S, Anti thrombin III, and others

- Retinal venous and arterial occlusion.
- Hemorrhagic retinal and choroidal detachment.
- Vitreous hemorrhage.

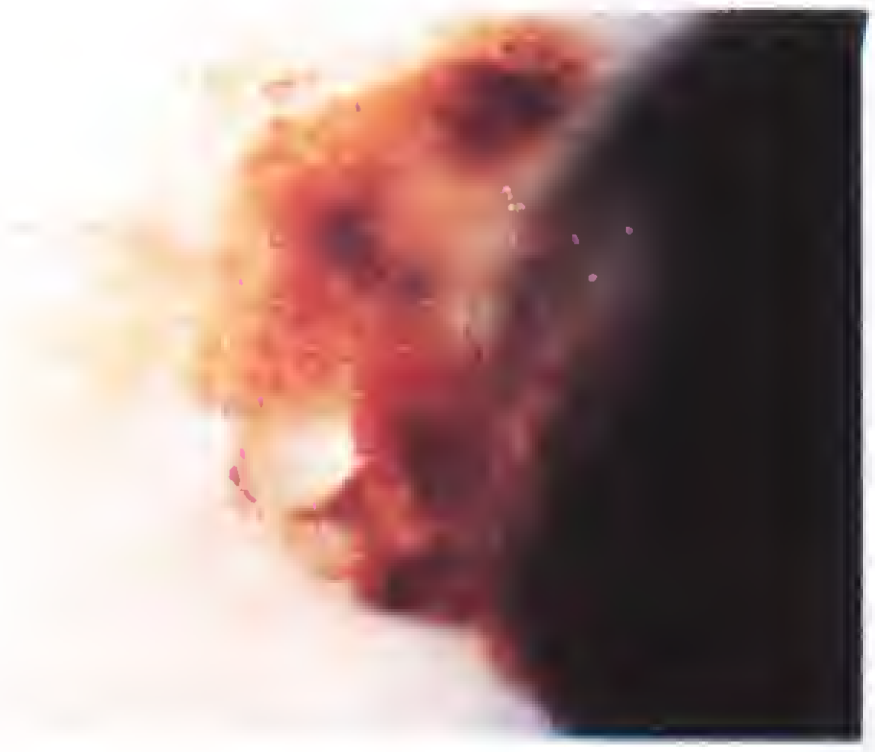
Homocysteineuria

- Lens subluxation.
- Glaucoma



Gauchers Disease

- Pigmented wedge shaped thickening of conjunctiva resembling pingecula.
- Pigmentation of corneoscleral junction.



RADIOLOGY READING ROOM DESIGN PART I : BASICS OF MODERN READING ROOM DESIGN.

Bakshi Jehangir MD; Ghulam Jeelani DMRD, MD

Introduction

Computerised imaging modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI) and digital radiography have permitted the development of filmless or virtual radiology departments in which all images are acquired and stored digitally by computers[1,2]. The use of radiographic film is gradually being replaced by digital imaging and the Picture Archiving and Communication System (PACS)[3-7]

Today, imaging is at the heart of the health care system, and the PACS-based reading environment is a critical componentof his system. In Radiology, group and team settings are becoming increasingly more important and a centralized, common reading area promotes collaboration and communication among radiologists[8].

As radiology departments make the transition from film-based, hard-copy reading, to filmless, soft-copy reading, our approach should be towards designing the modern reading room as a continuously evolving space that changes along with the progressive implementation of a fully-digital reading environment.

While only a few fully digital imaging departments exist at present, most are in the process of switching from film to digital reading, with their existing analog imaging equipment likely to be replaced and upgraded to digital over a period of time. However, a certain amount of film review may always be required, for comparison or referral, which will be phased out over a reasonable period of time, if ever[8]. Therefore, for the foreseeable future, radiology departments are likely to exist in a hybrid condition in which soft-copy and hard-copy readings co-exist, utilising both soft-copy workstations and film illuminators.

Reading Room Design

From a reading room point-of-view, this hybrid stage is the most challenging to design for because good space, lighting and acoustics for traditional hard-copy reading are quite different from the right conditions for soft copy.

The ideal reading room would enable radiologists to read in a comfortable ergonomic environment with controlled lighting and acoustics, and allow them to confer individually or in a group with colleagues and referring physicians. Three specific reading-room design elements[8] must be considered while designing the modern reading room:

- physical space demands,
- lighting, and
- ergonomics.

Physical space demands of the reading room include a work zone and an interaction zone. In the work zone, where primary reading activities take place, hybrid reading stations accommodate multiple film illuminators, digital monitors for viewing images, a separate computer workstation for information management and network communications and possibly also a separate teleradiology station within the team space. The work zone resembles an aeroplane cockpit with frequently used devices like trackball, keyboard, telephone, and microphone within arm's reach and should comfortably accommodate three or four people working together[9].

The interaction zone next to the workstations provides privacy for small group clinical conferences /consultations in the space beyond the reading area without disturbing radiologists in the work zone. Immediately beyond the interaction zone is group space with conference facilities for rounds.

In a PACS environment the single largest problem area in any reading room is related to lighting : glare, reflection, and inability to control lighting levels. All other factors being equal, radiologists tend to get more fatigued earlier in a filmless environment than in a film-based one, with room lighting being the single most important factor contributing to fatigue. The lighting needs for working with film and with a monitor are different. The challenge for reading-room designers is to balance the low lighting required for computer work while simultaneously allowing the lighting required for general work, such as that from nearby film illuminators or windows. Lighting that suits paperwork won't work around computers: the ambient lighting around computer workstations must be calculated so the contrast between the screen and surrounding surfaces does not create eyestrain, and yet the room must be dark enough and sufficiently free of glare to make the

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Dictation
Microphone

Figure A.Specialised dictation microphone for entering reports using voice-recognition technology.

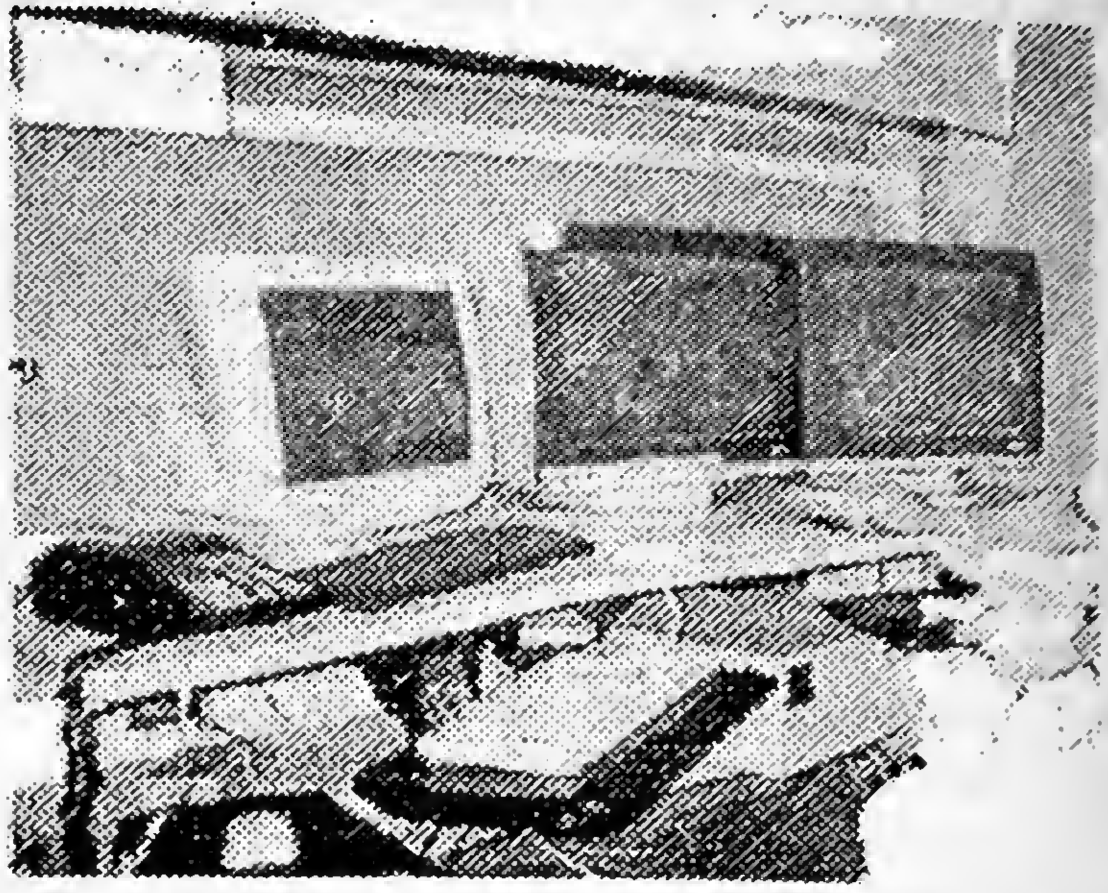

Figure B. Typical Workstation block in a modern Radiology Reading Room. Note the dictation microphone in the radiologist's left hand.

screen image readable[10].

Ergonomic design is very important in the hybrid reading environment providing both film-based and monitor screen viewing in a common workstation, since productivity will decline and health hazards like repetitive strain injuries will increase if proper consideration is not given to ergonomics. Poor ergonomic conditions such as improper lighting and glare can cause eyestrain while many back and wrist-related problems are linked to using computers repetitively. Three points of contact contribute to a healthy work environment: where your eyes interact with the computer monitor, where your fingers contact the keyboard, and where your body rests in its chair.[11] Furniture specifically designed for computer systems with adjustable seating, work surfaces, keyboards, and monitors can reduce the incidence of ergonomically caused health problems like repetitive motion injuries and fatigue.

The following guidelines are modified from the recommendations[8] of Morris A. Stein, the founding partner and president of the Stein-Cox Group, a Phoenix-based architectural firm specializing in health care facilities.

Physical Space

- Plan 125-sq-ft area minimum each for a hybrid reading station.
- Work surfaces should be 18-20 in deep — no more and no less.
- Consider adjustable, demountable furniture systems for reading.
- Select non-reflective finishes for walls and work surfaces.
- Use sound-absorbing materials for design details, including ceilings.

Lighting

- Avoid placing light fixture or film illuminator directly behind a computer monitor.
- Avoid film illuminators at right angles to computer monitors.
- Do not use a film illuminator to light the room.

Ergonomics

- Place frequently used devices within easy reach.
- Place the primary viewing device, film illuminator, or monitor screen at the optimal eye level height.
- When film illuminators and monitor screens are combined in one setting, place the illuminators above the monitors, with the surface face of the illuminators aligned with the monitors.
- Place phones, intercoms, dictation devices and control systems for lighting and electrical devices within easy reach.
- Study and implement human design factors and design standards.

RADIOLOGY READING ROOM DESIGN PART II : PLANNING A MODERN READING ROOM IN SMHS HOSPITAL

In the year 2001, the Department of Radiodiagnosis and Imaging of SMHS Hospital, the main teaching affiliate of Government Medical College, Srinagar, established a new Diagnostic Imaging Research Centre (DIRC) equipped with MRI, Spiral CT, mammography and ultrasonography units.

The DIRC is housed in a renovated section of an existing block of the hospital, built in the early twentieth century. Since the MRI, CT, and mammography machines were installed as turnkey projects, the civil and electrical works were executed by private contractors hired by the individual companies. The civil works, in particular, were designed around the existing structure and utilised available rooms, rather than being built from the ground-up as per the needs of a modern diagnostic centre. This lack of a central master-plan means that there is a serious lack of interaction between radiologists working in different sections leading to less-than-optimal productivity.

As part of the continuing upgradation of the DIRC, it is proposed to install a central PACS system, dedicated CT workstation, and a colour doppler unit in the near future. With a little planning and foresight this proposal can provide us with an opportunity to address the shortcomings by setting up a modern Radiology reading room as an investment in the future. Utilising the basics of modern reading room design as outlined in the first part of this article, the authors proposed the design illustrated at Figure C and D.

An existing space measuring 18 feet-by-20 feet with easy access from the central lobby of the DIRC will be used to set up the Radiology reading room. The MRI and CT installations are located nearby while mammography and USG units are located in adjoining rooms. Another adjacent room can be utilised for the installation of proposed colour doppler unit. This will allow easy connectivity between these modalities and the central PACS workstation. Since civil works usually form the major cost-component of any project, the savings are likely to be substantial and can be better utilised for proper ergonomic planning of the reading room.

The plan is discussed along the recommended[8] headings:

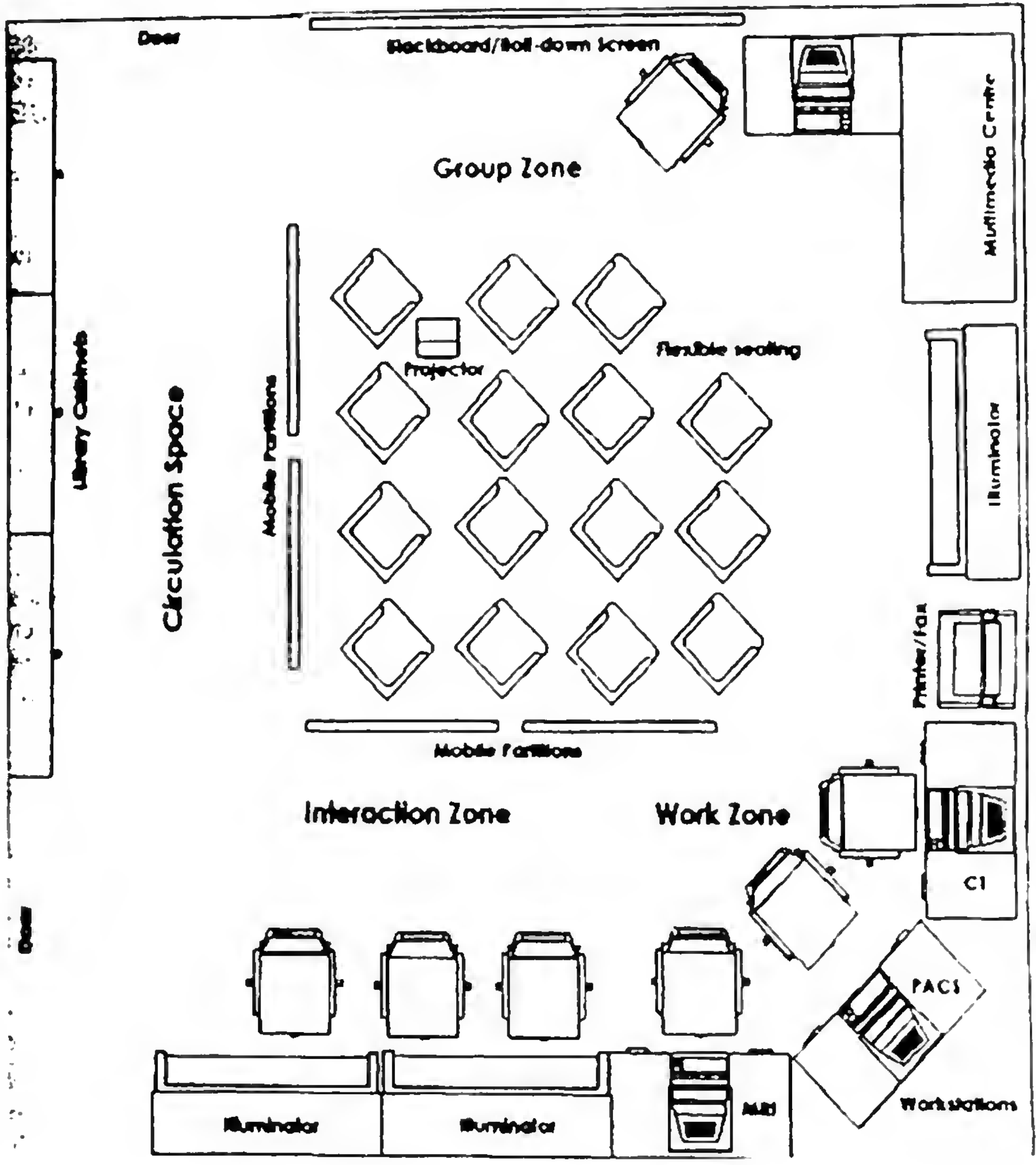

Figure C. Proposed Reading Room Design for DIRC.

Physical Space

The proposed work zone will include MRI workstation, CT workstation, and a central PACS workstation with access to electronic medical records, hospital intranet, e-mail, the internet, office applications as well as digital dictation, telephone, videoconferencing and telemedicine facilities. Film illuminators will be mounted directly above the monitors. The PACS workstation will be connected to the other workstations as well as USG, mammography and color doppler units for image retrieval and storage. Reports will easily be dictated using specialised microphones and voice-recognition technology, or will be typed and printed.

The interaction zone will have a film-viewing station including film illuminators, workbench, and seated and standing space for team consultation.

The group zone will include a film-viewing station, conference facilities like slide/multimedia projectors, blackboard, whiteboard and flexible seating space for a group of upto 15 people. This space will be demarcated from the work and interaction zones by adjustable mobile sound-absorbing partitions.

Library cabinets will be placed along one wall of the circulation space allowing comfortable movement within the reading room.

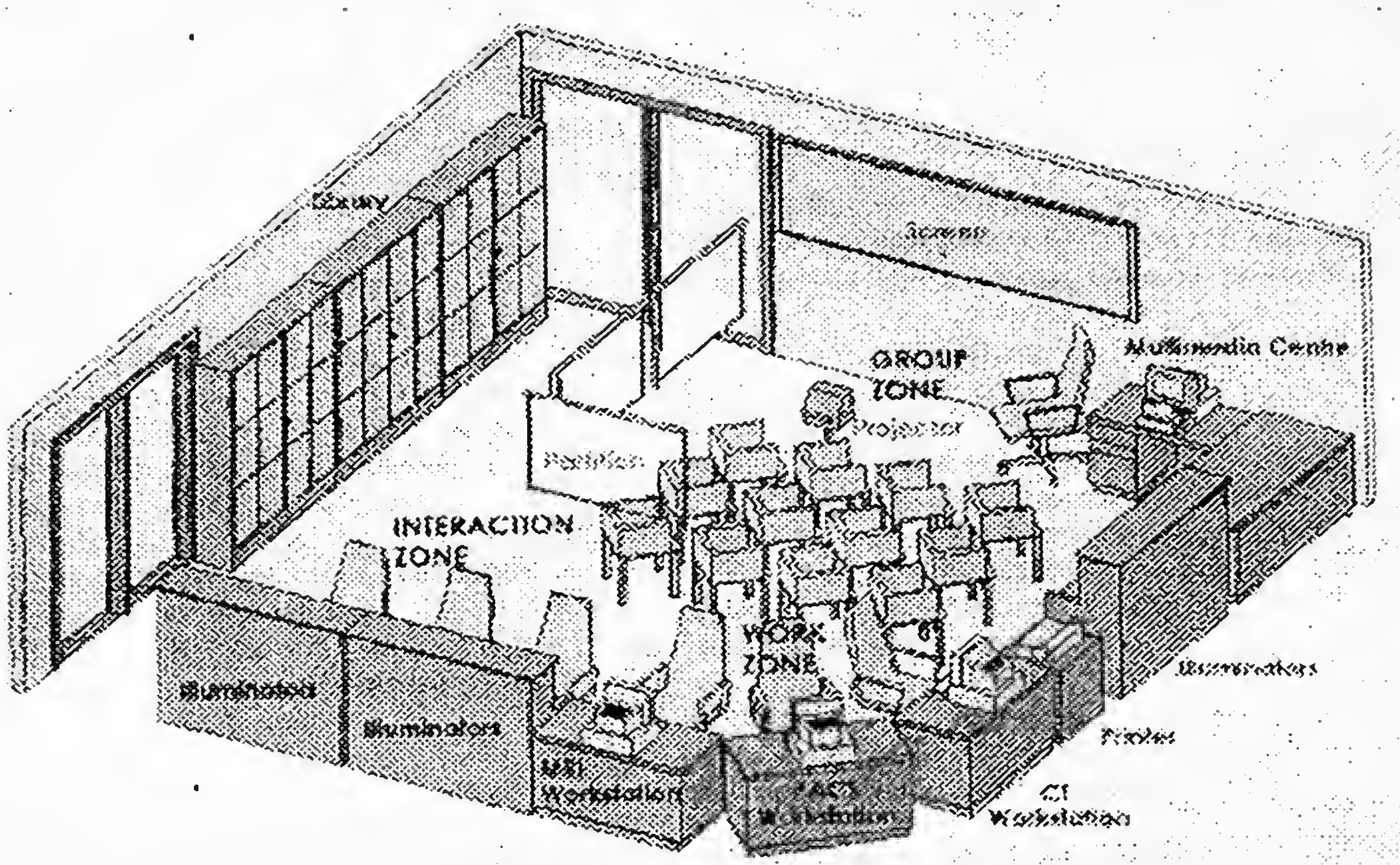

Figure D. Proposed Reading Room Design for DIRC (3D View).

Lighting

The switches for overhead lighting will be easily accessible and individually controlled dimmer switches will be used for control of ambient light. Film viewing/ reporting stations will have localised light sources and care will be taken not to place film illuminators directly facing the computer monitors.

Ergonomics

All tasks like film reading, PACS access, dictation, printing, telephony and lighting control will easily be accomplished at the workstation. Ergonomically designed computer tables and workbenches will be installed. Chairs will have lumbar support, adjustable heights, armrests, wheels and the ability to recline and swivel. Care will be taken to comply with the recommendations concerning optimum viewing angle and user-to-monitor distance.

Conclusion

This approach, if adopted, will help to boost productivity and patient care in the current imaging scenario of ever-increasing workload by providing a comfortable and ergonomic work environment to radiologists as well as providing scope for future expansion of the DIRC. Planning a state-of-the-art PACS reading room is more than design; it is the opportunity to reinvent[8].

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COMMUNITY-BASED DISABILITY MANAGEMENT: ARE WE READY?

Bashir Gaash; Ashfaq Ahmad; Rohini Bhan; Muzaffar Ahmad

Disability is largely a neglected problem in the developing countries. Part of the problem lies in the very erroneous structure of medical education which has all along been putting the onus of disability management on tertiary care services seeing no role for the primary care physician. Over the years, the management of disability has become synonymous with rehabilitation. The general practitioner, working in a rural set up, has conveniently been holding the ominous belief that he has no role to play in the management of disability. The centralized, institution-based services, being expensive, have remained out of reach to the vast majority of the disabled populations. Consequently, 98% of the disabled people in the developing world remain totally neglected.

Contrary to the commonly-held belief, disability is a colossal global health problem, which cant be tackled by the tertiary, highly specialized, institutional services alone. This has led to the worldwide awakening that all doctors working anywhere should be sensitized to disability and its management. The Government of India established an autonomous body, the Rehabilitation Council of India which, in addition to its regulatory functions, undertook the huge task of orienting each and every doctor of the country to disability management. In the J & K State the programme started in April 2000 and till March 2003, 510 doctors had already been oriented.

Each 3-day training session begins with pre-evaluation of the trainees about various aspects of disability, analysis of which reveals their pre-orientation awareness, beliefs & attitudes. The results are shared here to give an idea of the widely prevalent ignorance & wrong perceptions among the medical profession, which in turn shows the need and cost-effectiveness of such orientation trainings.

Discussion:

Analysis shows a poor awareness level and widely-prevalent misconceptions among participants (Table I).

Contrary to the common belief that disability is an uncommon problem, more than 300 million people suffer globally from one or the other form of disability. India accounts for some 70-100 million! Different studies in developed world have shown that some 7-10% of the general population have some form of disability.[1,2,3] Studies in some developing countries have found a lower prevalence which could be attributed to lesser community awareness and to scarce and inferior diagnostic facilities rather than to a real lower frequency. The actual prevalence in India has always remained unknown. Censuses have never been able to get the correct data since the majority of households don't voluntarily report a disability in a family member. The first reliable data on physically-handicapped persons came from the 15th National Sample Survey (1959-60), and the first comprehensive data was possible only during its 36th round (1981). In the 47th round (1991), information was also collected on visual & communication disability.(Table II). The latest (58th) round of National Sample Survey, whose analysis will give a more accurate contemporary picture, was concluded in December 2002.[4]

Another widely prevalent mis-belief among the participants was about the etiology of disability in developing countries. Although the main cause of disability in India, as in other developing countries, is communicable disease followed, in order by, malnutrition, poor quality of perinatal care, and accidents, none of our respondents could think of communicable disease as a cause of disability.

Only a few had heard about the Rehabilitation Council of India and still fewer knew about its varied functions. A mere 20% of the respondents knew that the 4 main types of disabilities covered under the programme are locomotor disability, visual handicap, speech & hearing impairment, and mental retardation.

The World Health Organization estimates show that, with the institution-based, high-tech, centralized rehabilitation along with their out-reach services, a mere 2-3% of the disabled persons in developing countries get any significant care, and that with such an approach it would take 100 years to catch up in time.[5,6] The logical approach, thus, would be the broad-based Community-based Rehabilitation (CBR), which aims to involve whole

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Table I: Awareness Level of Doctors About Disability & Its Management

S.No	Questions asked	Expected Response	Correct Responses (%)	Wrong or No Responses (%)
1	Are impairment, disability & handicap synonymous?	No	16.47	83.53
2.	What is the prevalence of disability?	5-10%	45.88	54.12
3.	Country with the largest number of the disabled?	India (100 million)	79.41	20.59
4.	What is the full form of RCI?	Rehabilitation Council of India	44.12	55.88
5.	What are the 3 main functions of RCI?	Counseling,Management, Rehabilitation	2.35	97.37
6.	RCI is the statutory body of which ministry?	Ministry of Social Justice & Empowerment	11.30	88.70
7.	Four main types of disability covered under the National Programme	. Locomotor Disability . Visual Impairment . Hearing & Speech impairment . Mental Retardation	20.59	79.41
8.	Commonest cause of disability in India?	Communicable Diseases	None	100
9.	Deficiency of which 2 nutrients can lead to common disabilities?	Vitamin A & iodine	27.05	72.95
10.	Main cause of blindness in India?	Cataract	54.70	45.30
11.	When does mental retardation occur?	During developmental period	45.88	54.12
12.	Two types of preventable mental retardation	IDD; PKU	11.18	88.82
13.	Two striking clinical features to differentiate mongolism & cretinism?	Mood & disposition; Protruding tongue	27.65	72.35
14.	Two most common causes of locomotor disability?	Cerebral palsy & poliomyelitis	12.35	87.65
15.	CBR stands for?	Community-based rehabilitation	12.35	87.65
16.	Rehabilitation of the disabled is primarily the responsibility of?	Community	14.18	85.82
17.	Main health outlet used as primary linkage in the referral for disability management?	PHC	31.76	68.24
18.	Role of medical officer in disability management?	Prevention, early diagnosis, early & appropriate referral	37.65	62.35
19.	The child who doesn't do well at school needs evaluation for?	Mental retardation (mild), Visual acuity, refraction errors, dyslexia, hearing(all)	41.18	58.82
20.	Two concessions given to the disabled by the Central or State government?	Job reservation; tax rebate; Study allowance; Fare allowance etc	54.70	45.30

Table II: Estimated number of disabled persons by type of disability (NSS 47th Round Estimates)

S. No.	Type of disability	Rural		Urban		Total	
		No	(%)	No	(%)	No	(%)
	Locomotor disability	6,807,000	1.07	2,132,000	0.96	8,939,000	1.05
2	Hearing & speech impairment	3,499,000	0.55	983,000	0.44	4,482,000	0.53
3.	Visual handicap	3,335,000	0.52	670,000	0.30	4,005,000	0.46
4.	Total estimated disability*	13,641,000	2.15	3,785,000	1.70	17,426,000	2.04
5.	Estimated 1991 census population of the Country	634,357,000		221,761,000		856,118,000	

(*Total estimated disability in the 47th round of National Sample Survey came to 2.04% of the country's population)

community in the care of a disabled person. The World Health Organization believes that at least 70% of the rehabilitation work can be dealt within the community as opposed to a mere 2-3% currently being tackled by the Institution-based Rehabilitation (IBR)[6]. The community doctor is the main, first or the only technical contact of the patient and the main health outlet used as prime linkage in referral for disability management is the primary health centre (PHC). Our study revealed that a mere 12% of doctors had heard about CBR and only 37% had any inkling about its role in this broad-based, community-oriented approach to disability management.

Conclusion:

The sheer magnitude of the disability problem and the plight of the "not-so-able" demands every doctor to shoulder his/her preventive, promotive & rehabilitative responsibility in a community-based approach. Since the main causes of disability are all preventable, the role of the doctor working in the community becomes all the more crucial. There is no period of life or stage of growth & development when a doctor can't help in prevention or management of disability.

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APPROACHING MODERN MEDICINE CHALLENGES THROUGH THE TRADITIONS OF IBN SINA (980-1036)

(IMANA - Ibn Sina Memorial Lecture)

Faroque Ahmed Khan, M.B., M.A.C.P.

It is, indeed a great honour for me to give the annual Ibn Sina Memorial Lecture, at the 36th annual convention of the Islamic Association of North America in the beautiful city of Anchorage, Alaska. This presentation commemorates the remarkable contributions and achievements of Abu Ali al Husain Ibn Abdullah Ibn Sina. Born in 980 near Bukhara in Uzbekistan, Ibn Sina was the foremost medical scholar, philosopher, and educator in the world at the beginning of the second millenium, a thousand years ago.

I have structured this talk as a conversation with Ibn Sina. Let us assume Ibn Sina has returned from "Barzakh" and is amongst us in Alaska. I will present some of our dilemmas to him and then seek his advice, specifically focused on the gathering at the annual IMA convention.

Before we do that, let's refresh our collective memory regarding Ibn Sina and the times he lived in.

Environment During His Time

Seventh-century Islam swept from Arabia through Egypt, North Africa, and Spain. Within one hundred years, most of the ancient Greco-Roman world had been transformed into a far-reaching Islamic society. Greco-Roman literature, works of Hippocrates, Aristotle, Galen were translated into Syriac, Aramaic, Persian, and Arabic. Libraries flourished; literature, poetry, and music were given priority in this Islamic society extending from Baghdad in the east to Aurtubah (Cordoba) and Tulaytilah (Toledo) in the west.

Education

Education was emphasized. In 980, the year Ibn Sina was born, every 12-year-old child in Baghdad could read and write. Caliphs' courts had physicians, scientists, and literary scholars, and intellectual discourse was intense and widespread. It was in this environment that Ibn Sina was born and flourished. Let's look at some of key accomplishments over his brief 57-year life span.

Ibn Sina was foremost medical scholar, philosopher, and educator. At eight years of age, he memorized The Holy Qur'an. He completed his medical studies by age 16. Over a period of 15 years he wrote the scientific encyclopedia "Al-Qanun" *(The Canon)*. This book remained standard text for 700 years. It was the *Index Medicus* of its time. *The Canon* was translated into Latin, Hebrew, and English. Ibn Sina was educated by and worked with Christians, Muslims, Jews, and Zoroastrians.

Ibn Sina diagnosed his own mortal illness almost 1,000 years ago. He retried to his home in 1036 and gave away all his possessions. He immersed himself in The Holy Qur'an, his poetry, and Islamic faith. During Ibn Sina's time, death lay in the domain of faith, not Medicine.

During the period - 800 to 1300 A.D., Islamic civilization was at its zenith and in the medical field the following five stand out as physicians "extraordinary".

Five Great Men:

AL RAZI-RAZES - Medicine, Epidemiology, Ophthalmology, Chemistry Bagdad, Iraq (841-926)
AL-ZAHRAWI - Pioneer Surgeon Cordoba, Spain (930-1013)
IBN SINA AVICENNA- Philosophy, Astronomy, Poetry Hamazan; Turjani, Iraq (980-1030)
IBN-RUSHDI AVERROES - Philosophy, Medicine, Law Granada, Span (1126-1198)
IBN-AL-NAFIS - Pulmonay Circulation, Blood Damascus, Cairo, Egypt (1208-1288)

Hospitals flourished, they were well endowed and patients had easy access to health care, physicians were licensed and a good example is:

Mansur Hospital in Cairo - 13th Century

- ◆ Case reports
- ◆ Bedside teaching

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The annual Ibn Sina Memorial Lecture was delivered by Dr. Faroque Ahmad Khan, Prof. of Medicine, State University of New York at Stony Brook, at the 36th Annual Convention of Islamic Medical Association of North America in Anchorage Alaska on July 26, 2003 - August 1, 2003. Dr Farooqe A. Khan is the President Islamic Centre of Long Island, New York. Reproduced with permission. Correspondence Dr. Faroque A. Khan. e-mail: farooquekhan@yahoo.com.

- Examinations for licensure
- Specialty Wards - fever, diarrhea, eyes, wounds.
- Elegant rooms, piped music
- Patients at discharge were given five gold pieces, to provide them financial support during convalescence.

Some Reasons for Success

- Encouraged learning and teaching from all sources
- Forbade destruction -ex: Mecca conquest
- Encouraged cleanliness and personal hygiene - ex: plague epidemics, epidemiology controls
- Tolerance for other religions

Few Reasons for High Standards

- Being part on an ascendant civilization
- High prestige of physicians
- Rulers' involvement in public service
- Adequate financing to run hospitals

Reasons for Decline

- Caliphate highly centralized, despotic, serverly orthodox towards any initiative and dissent - ex: printing presses forbidden.
- Imports encouraged; export forbidden
- Turks refused to adopt newer methods to control plague.
- Jannisaries destroyed state observatory in 1580, alleging that it caused plague.

Having learned a bit about this great civilization, let's now present some of our questions to Ibn Sina.

Questions for the Millenium

Patient's Rights	Bioethics
Transplantation	In Vitro Fertilization
Right to Life	Euthanasia
Alternative Medicine	Applied Gnetics
Cloning	Advanced Directive, etc.

I would also like to share with our guest, Ibn Sina, the dilemmas created by the rapid advances in technology; for example, the definition and moment of death.

> A consultant is called in regarding a devout, practicing Muslimah in her 80's suffering from a massive stroke and in an unresponsive state for over a week. Her six adult children, in the absence of an advanced directive, are not sure what to do and seek consultation. The consultant determines she is brain dead and suggests discontinuing ventilatory support. Some of the children question this evaluation as the patient has cardia erhythm and the urine bag is full, so how could she be dead, they ask. So in the current environment we are still debating and determining the moment of death-separation of soul and body-is it with brain death or cardiac function cessation or when breathing ceases?

Anohter case I would share with Ibn Sina would be:

> A 19-year-old male with cystic fibrosis requires repeated hospitalizations for breonchitis and pneumonia. A new, genetically engineered medication, Recombinant Human DNASE, is known to relieve severe respiratory problems. The monthly cost of this medicine is $1,200. The family asks The Islamic Center of Long Island for assistance. The ICLI executives ponder the dilemma of allocation of limited resources. They have an annual "discretionary" budget of $15,000 for such dispensation.

Advances in technology give us choices, both at the beginning and end of life, and the following dilemma faced by a young woman born without a uterus would be of great interest to Ibn Sina.

On Long Island-New York - twelve years ago, Martha and Jack explained to their fourteen year old daughter Joanne that she had been born without a uterus, making it impossible for her ever to become pregnant or bear her own children. Comforting her daughter, Martha promised, "If someday you and your husband want to have a family, I will carry your babies for youn." Three years ago Joanne married Robert and began thinking about the possibility of having children. When Joanne reminded her mother Martha of the offer she had made, Martha said "Off course I meant it". Though she was 48 at that time Martha was impregnated with embryo's created from Joanne's eggs and her husband Robert's sperm and she delivered not one but two babies. As a Muslim physician I was asked to comment on the question:

> Can Grandma Martha carry the fertilized ovum of her daughter, Joanne, and Joanne's husband, Robert? Joanne was born without a uterus.

Having presented our modern-day medical dilemmas, ranging from defining death, allocation of resources, and surrogacy, how might Ibn Sina respond?

I can assume since Ibn Sina was so well grounded in knowledge regarding The Holy Qur'an, he might start off bysharing some relevant Quranic verses with us.

Qur'an 5:32

And if any one saved one life
It would be as if he saved the life of the whole people.

Qur'an 45:26

Say: "It is Allah who gives you life, then gives you death;
Then He will gather you together for the Day of
Judgement about which there is no doubt;"
But most men do not understand.

Qur'an 23:100

"In order that I may work righteousness in the things I neglected"
By no means! It is but a word he says"
Before them is a partition till the day they are raised up.

Qur'an 2:195

And do not with you own hands cast youselves into destruction.

Qur'an 17:31

And slay not your children for fear of want.
We shall provide för them and you.
Lo! their slaying is a great sin.

Qur'an 17:23-24

Thy Lord hath decreed that ye worship none but Him,
and that ye be kind to parents.
Whether one or both of them attain old age in thy life,
say not to them a word of contempt, nor repel them,
but address them in terms of honor.

And, out of kindness, lower to them the wing of humility,
and say:
"My Lord! Bestow on them thy mercy even as they
cherished me in childhood."

Ibn Sina, besides being a *Hafiz-Qur'an*, was well-versed in the works of others who preceded him and his contemporaries. So, it's safe to assume that during his visit with us Ibn Sina would have read newspapers such as *The New York Times*, read a few books - perhaps mine, as well, *Story of a Mosque in America*, and read up on the accomplishments of others in the past millenium.

He would, I am confident, be very impressed with the advances in technology, particularly in the field of Informatics and the rapidly expanding application of the Internet. He would be appalled by the wide gap between the "haves" and have-nots." Two-thirds of the world's population lives in poverty, with 1.2 billion living on less than $1/day and 2.8 billion on less than $2/day.

IbnSina might start off by commenting:

Questions are always the same, because science is a synonym of wisdom and philosophy that yields knowledge that is certain by virtue of its insight into causes.

His overall impression of the community:

Ibn Sina would be impressed with the numbers and distribution of Muslims with Indonesia as the largest Muslim country and ruled by a Muslim female. He would quickly find out that Bangladesh, Turkey, and Pakistan also have or had female Presidents and Prime Ministers. An estimated Muslim population of over 1.2 billion is certainly very laudable and spread over the entire globe is indeed remarkalbe.

He would certainly comment and perhaps lament on the quality of Muslims.

He might say:

While your numbers are at an all-time high, the quality is another matter. You have just two Nobel Laureates - Abdus Salaam and Ahmed Zewail.

He would continue:

In our time (Al Razi, Zahrawi, Averroes, Nafis) the status of Muslim scientists was very different. Others used to look to us for guidance. Frankly, I was pleasantly surprised my book, "Al Qanun," remained a standard text -"Index Medicus" - for over 600 years and was translated into other languages.

Scholarship amongst Muslims and others must be put on the front burner - top priority - and I don't mean rote memorizing of facts, figures, texts. I mean real intellectual discourses, somewhat similar to the challenge Dr. Jamil Fayez presented at the IMANA meeting, when he challenged the validity of the commonly cited Hadith regarding the various stages of embryo-fetus infant.

Now some constructive critique, and I have broken it into "A", "B", "C". You like sound bites. In our time we used to sit and discuss, face-to-face, your lifestyles are very different. So, here they are:

"A"

Accent:	While speaking and expressing without accent is commendable, do not make correct accent an exclusive criteria for knowledge or piety.
Ancestry:	Bilal's example. Black Abyssinian slave became the muezzin and first treasurer of Islamic state - Islam is colorblind, focus on content and quality and not pedigree.
Agitation:	Lots of demonstrations, emotional outbursts. I don't see a well-laid-out strategic plan. I am glad IMANA President, R. Mir, has organized a strategic retreat-much needed.
Appearance:	Wearing a thobe, beard, turban is fine, but that shouldn't be a priority. As to Hijab, I will leave that for another day.

So, Ibn Sina might say, my suggestion is to de-emphasize the 4 "A's" - Appearance, Ancestry, Agitation, Accent.

"B":

Believing:	Quite a few Muslims are in hiding, afraid to live the faith in public - "closet Muslims." You have to believe in yourself, or you will suffer the fate of Muslims who migrated earlier and were totally assimilated and lost.

Belonging: Particularly for immigrants - Neither here nor there. Many of you are still wondering - Where is home? I like Hassan Hathout's definition of home- "where grandchildren live, not where grandparents are buried." Good man, Hassan Hathout. He left some important works for all of your. Faroque, I liked your book chapter where you incorporated the current healthcare crisis and some solutions in describing a *Khutbah* at ICLI. You must get engaged in addressing local issues. "Thinking global but act local."

Behaving: Now I was appalled to see the scene on Firdays in several mosques. You have these four-wheeled, fast-moving, gas-quzzling, environment-polluting machines - cars. We used to live close to the mosuqes, go for prayers on foot or horses, and made sure the animals were properly secured. I heard several neighborhoods objected tothe parking on Firdays around mosques. You can do better and show civic sense; that's your Jihad - winning the hearts and minds of your neighbors.

Boring: I attended a few Friday *Khutbahs* - too much vitriolic language, anger, blaming others, past glory, very little focus on current issues and problem-solving. Your kids are tuning out. Glad to know that ISNA had made Imam training the top priority in its plan.

So, I have been rough on you, so far:

Four "A's:: Accent, Ancestry, Agitation,Appearance

Four "B's": Believing, Belonging, Behaving, Boring

Now, let met leave you with four "C's to work on:

"C":

Competence: Excel in whatever you do - school, college, or profession. I was pleased to learn that one of your former IMA speakers, Elias Zerhouni, an Algerian Arab Muslim, was selected as head of NIH, based on his *competence* and *contributions* in science.

Courage: You must speak out for justice, not just for Muslims but for all. the honor killings, sectarian violence, lack of religious facilities for non-Muslims in some "Islamic" countries is wrong. You must take the lead in speaking out about these injustices.

Character: Syed Ali, a gas station attendant in Brooklyn, saved a synagogue from burning. The rabbi said, "Ali is my hero." You must show the good side of Muslims, and that's by action and I use Ali's very practical example.

Clarity: You informed me what the Director of the FBI, Mr. Mueller, told you about the vitriolic and hateful literature being circulated in some Islamic schools and mosques. In fact, Faroque, you showed me, in a translation of *The Qur'an* by Mohsin Khan in *Ayah7 of Surah Fath*, the translators have added to the words "gone astray" (like Jews and christians). Such literature needs to be removed from circulation.

When I wrote Al Qanun, I synthesized work of Greek-Roman period, and crystallized it and incorporated many parts of it. Nothing wrong in learning from others and adopting what's useful.

Now, let me conclude with a few other remarks. During my time, a thousand years ago, we had a close working relationship with Jews and christians. In fact, Maimonides is a product of your time. Even Abba Eban, Israeli diplomat, stated the golden period for Jews was during the Muslim rule in Spain. He noted in his autobiography two periods when Jewish culture truly flourished. First and greatest was during the 400 years of Islamic Renaissance, and the second one after the Jewish migration to the USA.

Out of curiosity, I looked up the current status of the Jewish community and came across this book. This small group of 13 million amongst five billion (less than 1%) has accomplished a lot, and it just didn't happen. A lot of work went into it. In fact, the seven secrets I am going to share with your group are from this book. There is much to learn from this. There are rather impressive accomplishments described in this book, "The Jewish Phenomenon," by Steven Silbiger.

The seven secrets described by Silbiger in his book are fairly simple, and you folks can learn from this experience.

1) Understand that Real Wealth Is Portable; It's Knowledge,
2) Take Care of Your Own and They Will Take Care of You
3) Successful People Are Professionals and Entrepreneurs
4) Develop Your Verbal Confidence
5) Be Selectively Extravagant but Prudently Frugal
6) Celebrate Individuality: Encourage Creativity
7) Have Something To Prove: A Drive To Succeed.

Let me also advise your to make sure you combine your work with other activities so as to lead a balanced life. I used to enjoy poetry and philosophical discourses with colleagues. I found it quite relaxing.

Let me now conclude with a few practical suggestions:

I. Linkage and collaboration with other medical organizations - a good example would be the mini-fellowship program of the American College of Physicians. There is no reason why IMANA can't be a partner in this program.

2. Quality of Care and Setting Standards

   I noticed many of your have immigrated from other courntries. You are well aware of the highly variable standards and quality of care provided. With some well-thought-out programmes, you can make a difference. The Ghulam Rasool Essay Contest in Kashmir, now in its fourth year, has provided encouragement to quite a few young medical students and physicians in training.

3. Tolerance for Other Faiths and Views

   Some of you will be surprised to learn that 50 years before my birth, in January 929, Abd Rahman III declared himself the Caliph in Spain-Commander of the Faithful, Caliph of the Islamic World. Successor to the Prophet at the Head of the Entire Muslim Community.

   A remarkable historical fact is that Abd Rehman's Prime Minister was a Jewish rabbi, Hasdai. My guess is that most of you didn't know this fact. You have a very long and rich tradition and history of tolerance for faiths. Be proud of it, share it with others.

   I really enjoyed reading the book "Ornament of the World" by Rose Marie Menocel, in which she describes the great Andulasian civilization where Christians, Jews and Muslims lived together in peace and excelled in doing good. I particularly liked the chapter "Grand Vizier in a Grand City." This chapter is devoted to the rabbi who was the Prime Minister of Abd Rehman.

Let me, Ibn Sina, conclude with the eternal message from *The Holy Qur'an*:

Qur'an 5:48

If Allah had so willed, He would have made you a single People,
But (His plan is) to test you in what He hath given you:
So strive as in a race in all virtues.
The goal of you all is to Allah:
it is He that will show you the truth of the matters in which ye dispute.

Clearly Muslims have a challenge ahead of them. Hopefully my (Ibn Sina's) brief observations will be helpful in providing some guidance. May Allah bless all of you.

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MID-TERM CME UROOLOGY 2003
29-30 AUGUST 2003

29th & 30th AUGUST
GOVT. MEDICAL COLLEGE SRINAGAR
GOVT. MEDICAL COLLEGE

The post graduate department of Surgery Government Medical College/SMHS Hospital organized a North Zone Mid Term CME for the first time in the state of Jammu & Kashmor. Prof. Ghulam Jeelani, Head of the Department Surgery was the organizing Secretary for the said conference which was held in the auditorium of the Govt. Medical College. The two day conference was attended by nearly 400 delagates from the state of Jammu & Kashmir and other northern states of the country. Eminent guest faculty from urological institutions from abroad as well as from the Northern States and the local talent gave guest lectures covering all the aspects in Urology. There was also a free paper session for post graduate scholars. Video Session conducted by eminent urologists demonstrated various urological techniques for the benefit of the surgeons.

The conference was inaugurated by the Hon'ble Finance Minister, Mr. Muzaffar Hussain Beigh and Mr. Gaffar Sofi, Minister for State for Health and Medical Education.

MEDICINE UPDATE-2003
27-38 SEPTEMER, 2003

MEDICINE UPDATE-2003
DICINE UPDATE-2003
CME PROGRAMME

The department of Medicine Govt. Medical College, Srinagar, orgasnized a CME (Continued Medical Education) programme in collaboration with the Medical Council of India (MCI). The two day conference was attended by about 500 delegates from across the country. Sessions covering various specialities, simultaneously run in two halls covered many of the specialities in medicine particularly Cardiology, Gastroenterology, Endocrinology, Oncology, Hematology, Pulmonology and Nephrology.

Awards for Excellence

BEST MAGAZINE AWARD FOR JK-PRACTITIONER

Prof. G.M. Malik Chief Editor,JK-Practitioner receiving the best medical magazine award 2003 from the Doctor's Association Kashmir. (DAK) in a function held on 4th September 2003 at Tagore Hall Srinagar

Dr. Zaffar Abbas Executive Editor JK-Practitioner receiving the award for "EXCELLENCE IN EDITORIAL SKILLS" from the chief Minster Mufti Mohammad Syed on the annual college day 2003 of Govt. Medical College Srinagar. Dr. Abbas is also the Associate Editor KASHMED the annual college magazine and the editor of MFA News Bullentin of the Medical Faculty Associaton GMC Srinagar

16th INTERNATIONAL
GENERAL MEDICAL
PRACTIT

Prof. G.M. Malik receiving S a Momento at 16th Annual Conference of General Practitioners of Pakistan, held at Lahore.

IMA DELEGATION TO LAHORE

Indian Delegates at Lahore

NAL
CONFEREN
PRACTITIONERS

Prof. G.M. Malik Chairing one of the sessions at the conference

A delegation of Indian Medical Association (IMA) attended the 16th.Conference of the General Practitioners Pakistan at Lahore. The 32 member group led by Dr.Jagit Singh ,Honorary Secretary of IMA College of general practitioners was on a peace and goodwill mission to Pakistan on the invitation of Pakistan Medical Association (PMA).

The IMA signed a draft memorandum of understanding with PMA to explore common areas on interest where medical fraternity from both the countries can contribute towards medical education, research, drugs, equipment and other related fields.

Dr.PV George Elected National President of IMA

Dr.Puthenkandathil Varkey George took charge as the National President of IMA on 30th.December 2003 during the 78th.All India Medical Conference at Guntur, Andhra Pradesh. Dr.VP George,hailing from Kerela has been working actively for IMA both at the state and national level since 2 decades. He is s senior consultant Gynaecologist practicing at Kannur. He won the national president election with a whopping majority securing the maximum number of votes (67,281),an all time record in the history of National President election.

CONDOLENCES

The Editorial committee of JK-Practitioner express deep sorrow and convey their condolences to:-

1. Dr.Faroque A Khan and Dr.Arfa Khan on the demise of **Haji Ghulam Hassan Khan**. Haji Sahib who passed away on December 31th., 2003 at Srinagr was the first Chief Engineer of J&K State.
2. Dr.Sajjad Peerzada (Cyber Scan, Karannagar) on the demise of his father **Peer Hisamuddin** a well known political figure of Kashmir.
3. Dr.Sadiq Rivzi (Budgam) on the demise of his brother **Rivzi Sahib**, former Chief Justice of J&K High Court.
4. Family of **Dr.Syed Zubair Ahmad** (Consultant Radiology at JVMC) on his death in a tragic road accident.

We pray to Almighty to bestow peace upon thedeparted souls and give courage to the berveaved families to bear the loss

Editorial

ADVERSE DRUG REACTION MONITORING WITH A KASHMIRI PERSPECTIVE - NEED FOR AN URGENT INITIATIVE

Geer Mohammad Ishaq, M Y Shah, Parvaiz A Koul, Shafiqa A Tanki

With the addition of a multitude of drugs to the physicians armamentarium, the treatment of many hitherto uncontrollable diseases has become possible. Every progress has however a price to pay, new drugs have led to a new group of diseases- the iatrogenic diseases. Ironically these may be called as 'Diseases of Medical Progress'. "Primum non nocere " - first of all be sure you do no harm - has long been a principle of the practice of medicine, and one of the greatest hazards in the use of potent drugs is their inherent toxicity and the dangers of the drug appear to be greater than ever before. The last few decades have seen an immense growth in availability and consumption of medicines. Whilst most consumers derive far more benefit than harm, a proportion of patients experience Adverse Drug Reactions (ADR) from the use of medicines at recommended doses and frequencies. For some such undesirable effects are sufficiently severe to require hospital treatment and a few even die.[1]

An Adverse Drug Reaction (ADR) has been defined by the World Health Organization as " a response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of a physiological function." This definition excludes intentional or deliberate overdose and drug abuse.[2] The present day Adverse Drug Reaction problem is the outcome of a variety of factors e.g., availability of a large no. of drugs to the doctors, the inability of any physician to be expertly informed on all aspects of all new drugs, and the pressure by sales promoters to create a demand for the drug, canvassing by detailmen and even colleagues, and the persuation of patients themselves to use the new drugs on them promptly before much becomes known about the human toxicity of the drug.[3]

Recent works have suggested that:-

Adverse Drug Reactions are responsible for 11.5 % of hospital admissions in Norway, 13% in France and 16% in UK.[4,5,6]

6.7 % of hospitalized patients suffer SERIOUS whereas 0.32% suffer FATAL Adverse Drug Reactions.[7]

In 1994, overall 2216000 hospitalized patients had serious ADRs and 106000 had fatal ADRs, making these reactions between the fourth and sixth leading causes of death.[8]

Prospective studies by Tafreshi et al have shown that medication-related visits (MRVs) to hospitals are most often caused by an ADR followed by over-prescribing of the correct medication. The most common medications involved were cardiovascular agents. The preventable MRVs were mostly due to non-compliance issues, inappropriate prescribing, inappropriate monitoring and lack of patient education.[10]

During fiscal year 2001-2002, the Pharmacy and Therapeutics subcommittee of the University of Iowa reviewed 356 ADR reports submitted to its Hospitals and Clinics ADR Reporting Program.

Speciality-wise classification of these ADRs was given as under:-[11]

CNS agents	-25.2 %	Anti-infectives	-24.5 %
CVS agents	-12.6 %	Antineoplastics	-3.8 %
Serum	-3.6 %	Hormones	-3.8 %
G. I. Agents	-1.4 %	Blood formn.	
& coagulation	-12.1 %		
Unclassified	-12.9%		

There are some limitations to the drug approval process. With most drugs, approval for marketing is granted following phase III clinical trials which are conducted

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in relatively small number of patients (usually involving hundreds and not thousands) under conditions that are not clinically routine, and often exclude patients with co-morbidities and co-medications.[12] Information about rare but serious adverse reactions, chronic toxicity, use in children, elderly or pregnant women or drug interactions is often incomplete or not available after clinical trials. At least, 30,000 people need to be treated with a drug to be sure that one does not miss at least one patient with an ADR which has an incidence of 1 in 10,000 exposed individuals.[13] The safety profile of a drug evolves over its lifetime on the market. Even after almost ten years experience or longer, new information that will impact the clinical use of a medicinal product can be detected. There are several examples of such drugs that were withdrawn from the markets decades after their approval. For example, anti-depressant drug Nomifensine was introduced in Germany in the year 1976 and prescribed to an estimated ten million patients prior to its worldwide withdrawal from the markets by WHO in 1986. Consequently, all medicinal products need to be continually assessed for safety within the context of their perceived benefit.

Morever incidence of ADRs imposes a huge burden in terms of costs on our healthcare system. In a recent Dutch study, the cost of ADRs to the Dutch healthcare system in 1998 was calculated to be in the range of whopping Euro 186 million to Euro 430 million a year.[14] The annual national cost of drug-related morbidity and mortality was estimated by Bates et al at $ 76.6 billion, with the majority ($47 billion) related to hospital admissions associated with drug therapy or the absence of appropriate drug therapy.[9] The overall impact of ADRs on England has been estimated to be at a cost of about 380 million pounds a year to the NHS in England. One in 10 of all NHS bed days are taken up by the consequences of ADR or hospital-acquired infection.[1] Research in US to determine the hospital costs directly attributable to ADRs estimated that they may lead to an additional $ 1.56 to $4 billion in direct hospital costs per year.[15] Therefore estimation of incidence and prevalence of adverse drug reactions are necessary to assess the consequences and impact of these effects in a population since these estimations reveal the magnitude of ADRs in terms of mortality and morbidity.[16]

In India, Drugs Controller General has approved 148 new drugs belonging to different pharmacological classes for use between Jan., 1999 to Dec., 2002. However, cardiovascular agents, proton-pump inhibitors like Omeprazole, NSAIDs like Nimesulide, anti-allergics like Loratidine, Terfenadine and many such drugs continue to be used unabated in India without sufficient monitoring for their adverse effects in spite of several reports of their adverse effects pouring in from around the globe.[17]

Kashmir valley presents a huge market for drugs. Drugs in very large quantities are sold throughout the valley every month. But unfortunately, there is no provision to monitor these drugs for their adverse effects vis-a-vis their therapeutic uses, in any of our major hospitals. Literature survey on Toxline, Medline, Biological and Chemical Abstracts between 1966 to 2003 has revealed that very few reports of adverse drug reactions from Kashmir valley are currently available. As a result, there is complete derth of information on risk-benefit ratios of drugs that are being widely used throughout the valley. Though most of the major hospitals outside the valley have centres for adverse drug reaction monitoring as well as drug information services, there are no such services or centres existing in our valley.

Estimations of incidence and prevalence of ADRs are necessary to assess the consequences and impact of their effects in a population. These estimations reveal the magnitude of ADRs in terms of mortality and morbidity. Studies have indicated that pharmacists should participate actively in ADR monitoring.[18] In U.K., Yellow-card and Black-triangle schemes have been implemented to ensure enhanced reporting of adverse drug reactions wherein pre-paid yellow post cards are provided to doctors for ADR reporting and inverted black triangles are assigned for a period of approx. two years to drugs new to the U.K. markets or established drugs available as new formulations. Hospital Pharmacists have been invited to take part in the yellow-card scheme from April 1997 and Community Pharmacists from Nov. 1999.[19]

It has been a general observation worldwide that physicians do not routinely report ADRs and USFDA Medwatch programme has attributed following reasons to under-reporting of ADRs by the Physicians:-[20]

not part of regular routine - 20 %
lack of time to complete ADR forms - 15 %
inability to determine causality - 13 %
most reactions are already reported and not unique - 10 %
reporting to govt. agencies is too much work - 9 %
responsibility rests with the attending physician - 7 %

Under these circumstances, it is for the Pharmacists and the Clinical Pharmacologists to take an initiative and venture into ADR monitoring studies in association with other clinicians so that due attention is paid to such important aspects of our healthcare system and more and more adverse reactions are brought to surface that otherwise go unnoticed in our clinical settings.

Drugs that have been recently marketted (< 5 years) with limited post-marketing experience and cause potential safety concern from pre-market review ; marketted drugs for which there are emerging safety concerns, new serious adverse drug reactions that are unlabelled in the product monograph and even the drugs that bear no reports of any adverse reactions from anywhere else in the world could form a part of Adverse Drug Reaction Monitoring Programme in Kashmir Valley possibly because there are differences among countries and even regions within countries in the occurrence of ADRs and other drug-related problems. This may be due to differences in:

diseases and prescribing practices
genetics, diet, traditions of the people
drug distribution and utilization pattern including indications, dose and availability

use of traditional and complementary drugs (e.g., herbal remdies) which may pose specific toxicological problems, when used alone or in combination with other drugs.[21]

In light of the fact that about 30-80 % of Adverse Drug Reactions may be preventable [22], comprehensive and ongoing ADR monitoring, evaluating and reporting programs need to be initiated that should focus on the assessment of incidence, prevalence, category, severity, preventability, costs and burdens of Adverse Drug Reactions. This will help ensure that patients receive safe medicines and mortality/morbidity due to ADRs is considerably reduced.

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POST TRAUMATIC STRESS DISORDER: AN OVERVIEW

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Diagnostic and Statistical Manual of Mental Disorders IV edition (1) defines post traumatic stress disorder (PTSD) as set of symptoms which occur after "the person experienced, witnessed or was confronted with an event or events that involved actual or threatened death or serious injury or a threat to the physical integrity of the self or others" and "the person's response involved. intensive fear. helplessness or horror .In addition to a positive traumatic event it requires the presence of one "re-experiencing", three "avoidance" and two "increased arousal" symptoms for diagnosis. PTSD has a global significance. and its impact in countries that have been experiencing repeated disasters and social unrest for many years could be a large public health problem.

HISTORICAL BACKGROUND:

Awareness of the role of psychological trauma as a contributory factor in psychiatric disturbances has waxed and waned throughout the past century. (2). The study of the traumatic origins of emotional distress started during the last decade of 19th century when Charcot first proposed that the symptoms of what was then called "hysterical" patient had their origin in histories of trauma. Specific categories such as rape trauma syndrome (3) and combat Neurosis (4) paved the way for recognition of a general category of PTSD in DSM-III American Psychiatric Association (5) introduced after the description of post Vietnam War syndrome. The interest in PTSD has increased tremendously in past 20 years. Important advances have been made in the understanding of the nature and treatment of PTSD during these two decades.

EPIDEMIOLOGY

Traumatic events are very common in most societies, though prevalence has been best studied in industrialized societies only particularly in USA. (6). Helzer et al. (7) in their assessment of PTSD in the St. Louis portion of the epidemiological catchment area (ECA) survey in USA indicated life time prevalence of PTSD as 0.5% for males and 1.3% for females. Subsequently another study reported life time prevalence of PTSD among adults as 9.2 %.(2). In a community sample of adolescents the life time prevalence of PTSD was reported as 6.3 %.(8). Kessler et al. (9) observed a life time PTSD prevalence of 2.8% and 10.3% for males and females respectively.

The prevalence of PTSD is obviously greater in the populations at risk. The National Vietnam Veterans Readjustment Study found a life time prevalence of 30.9% for males and 26% for female veterans. (10) Another study noted a prevalence of 15% among Vietnam veterans 20 years after war (11). PTSD prevalence rate of47% and 50% in former prisoners of war of World War II was respectively reported nearly after 40 years after their imprisonment during the war (12,13). 65% of the Bosnian refugees re-settled in the US suffered from PTSD, while 72.8% of Palestinian children exposed to war trauma experienced PTSD (14,15). Some communities are reported to be at higher risk of PTSD. In South American Indian community, the prevalence of life time PTSD and of exposure to a traumatic event were higher than general US population. (16)

It is unclear whether these US results generalize to other developed countries (2). The situation is almost certainly quite different in developing countries where large proportions of the populations have been exposed either directly or indirectly to terrorist attacks, torture, sexual assault and forced relocation. (17,18,19). Entrapped and suspended from their past, refugees can develop disabling symptoms that may mimic

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post traumatic stress disorders (20). Estimates of the prevalence of PTSD in the general population of the countries other than America are lacking (21). To the best of our knowledge there is no published or detailed studies available so far from India except a few national and international conference presentations (22-28). This extreme paucity of scientific literature is also clearly reflected in the presidential address at the 56th annual national conference of Indian psychiatric society of 2004 (29). The president referring to this subject commented " the published Indian data in this area is dismally minimal .In their study. Margoob et al. (30) reported significant increase in the number of individuals seeking treatment at a general hospital psychiatry unit (GHPU) in Srinagar. Their number has risen from a total of 1762 in 1990 to 37860 in the year 2001. This marked increase of attendance in a psychiatric OPD cannot be possibly explained by any other factor except the growing impact of violence. In the year 2001 a significant number of patients (2.38 %) were diagnosed to be suffering from PTSD. Among these 68.2 percent had immediate onset and 31.8 percent had delayed onset i.e. onset after 6 months of the traumatic event. Gautam et al (31) in their study on the victims (n=31) of a bomb blast in a bus caused by terrorist activity reported 35.4 percent of psychiatric morbidity at day 3 and 29.3 percent after 2 weeks. After 2 weeks the most common ICD10 psychiatric diagnosis was PTSD (12.9 %) followed by depression (9.6 %) and dissociative amnesia (6.4 %)". Other reports on various disasters in India if pursued with scientific zeal can also pave a way for valuable research in this important area (32-34)

ETIOLOGY AND RISK FACTORS

There is compelling neurobiological reason to believe that PTSD emerges in the aftermath of traumatic events given the importance of traumatic memory to the etiology of PTSD (35). Two conflicting views have dominated the literature on the etiology of PTSD. Residual stress hypothesis (36) maintains that PTSD is caused primarily by trauma and can last indefinitely even in people with traumatic personality adjustment but others (37) differ and propagate stress evaporation hypothesis which suggests chronic PTSD develops only in people with preexisting weakness. Similarly many people have debated whether PTSD is a normal response to trauma or an offshoot of pre existing psycho-pathology (38-40) Obviously according to ICD-10 or DSM IV criteria 'A' is to be fulfilled to consider the presence of PTSD. But it was always there that not all persons who are exposed to trauma develop PTSD.(41) Examining the longitudinal course of PTSD raises a series of conceptual issues about the relationship between PTSD and other disorders and the way in which risk factors influence vulnerability to the disorder and its remission (40).

PTSD may be a disorder in which there is failure of the resolution of the acute stress response or in the more toxic forms of post traumatic adaptation, a progressive recruitment of instabilities of the underlying neurobiological system (42). This possibility raises many interesting quesions about the relationship between the acute psychological state of an individual, his or her neurobiological system, and the capacity for preventive treatment interventions to be of benefit in the immediate period after a traumatic experience(43).

ENVIRONMENTAL FACTORS

A study in 1990 found that combat exposure remained strongly related to PTSD symptoms even after effects of socio-economic status race, age and pre service mental health status were controlled for (11). A history of prior exposure to trauma is an extremely potent risk factor for PTSD (44) and previous exposure to trauma signals a greater risk for PTSD from subsequent trauma (41) and Multiple previous events had stronger effect than a single previous incident (41). Family instability is associated with increased prevalence of PTSD (39) where as a good social support is associated with lower levels of symptoms (45).

PRIOR PSYCHIATRIC DISORDERS

Contrary to earlier results Neuroticism and past history of treatment for a psychological disorder were better predictors for post traumatic morbidity than the degree of exposure to the disaster or loss sustained (46). A recent study reported that a prior affective substance abuse represented risk factor for PTSD(41) and concluded that a psychiatric history per se was a strong predictor of PTSD than having a history of any one of the specific disorders. Another study(47) reported a high rate of PTSD among those hospitalized after acute psychiatric episode, 67% of the sample had PTSD at the discharge time and 50% at 4-6 months follow up.

PERSONALITY

Pre military personality profile can affect the vulnerability to life time PTSD symptoms in men exposed to combat (48). Neurotic personalities have also higher risk of developing PTSD.(49)

DEMOGRAPHIC VARIABLES

Gender is an extremely salient risk factor for PTSD(50). Although the life time prevalence of exposure and number of traumas was lower in females, the risk of PTSD was two fold than males after adjusting for sex distribution of trauma types. Risk of acute PTSD after motor vehicle accident is 4.64% times greater for women than men (51). In general women were 2.38 - 2.49 times more likely to develop PTSD than men after exposure to similar trauma. (8,52)

An explanation of the sex difference was primarily attributed to because of the assaultive /violence in females(49) and differences in the peritraumatic dissociation in genders(53). Ethnic minorities (40), asylum seekers (54) are at higher risk for PTSD. Lower levels of education and income are risk factors(55,46).

IQ AND INTELLIGENCE

A study (56) has found that low scores in pre military arithmetic aptitudes test were associated with chronic PTSD. Lower intelligence was a risk factor for PTSD symptoms and cognitive variables may affect the ability to cope with trauma, thereby affecting whether a person develops chronic PTSD(57).

Another recent study(58) again showed that a lower pre combat intelligence was a risk factor for PTSD symptoms even after adjustment for extent of combat exposure. A study of Chronic PTSD patients(59) observed PTSD cases had higher neurological sign scores than other people. Subjects with PTSD report more neurodevelopment problem and more childhood attention deficit hyperactivity disorder symptom and had lower IQ, all of which were significantly correlated with neurological soft signs.

DISSOCIATION

A peritraumatic dissociation appears to be an important risk factor for development of PTSD(60). A prospective study(61) concludes that peritraumatic dissociation has strong association with late development of PTSD. Early dissociation and PTSD symptoms can help the clinician identify subjects at higher risk of PTSD. Studies in Vietnam war Veterans have found that veteran with PTSD had experienced levels of dissociation symptoms during combat that were higher than those reported by veterans with out PTSD(62) Marmar(63) reported that peri traumatic dissociation contributed to PTSD in Vietnam war Veterans more than contribution from combat exposure. Similarly studies in Cambodian refugees have shown a relative relationship among trauma severely dissociation symptoms and post traumatic stress(64). Symptoms of dissociation also appear to be significantly related to somatic complaints reported by victims of trauma. A studies of a variety of traumatized populations have shown that dissociation is a significant predictor of subsequent development of PTSD. These include study on North sea oil rig disaster(65) students in Loma Prieta, California .earthquake(66) and kidnapping victims held hostage(67). At present it is not known whether the propensity to dissociate is result of trauma exposure or whether it represents a trait that predisposes an individual to dissociate during stress.

BIOLOGICAL

It is difficult to interpret the increased susceptibility of the family members to PTSD following traumatic exposure as evidence of biological/genetic factors(68). Severe abnormalities have been found in PTSD patients. Subjects who developed PTSD had higher heart rates at presentation in emergency department than those who did not(69). Pitman(70) had already proposed that elevated norepinephrine during trauma may result in over consolidation of memory and subsequent symptoms. Small hippocampal volumes reported in patients of chronic PTSD(71) has been taken as an evidence that stress related disorders induce hippocampal volume loss(72-74). An alternative possibility suggested is that small hippocampal volumes predispose to development of disorder aggravated by stress(71,73).

In human with mood and anxiety disorders small hippocampal volumes have been taken as evidence that excessive stress levels of cortisol induces hippocampal loss(75). In fact the alterations that have been noted in PTSD differ from those that have been described in most studies of the normative stress response. Furthermore the HPA axis finding in PTSD are distinct from those reported in other psychiatric conditions even with conditions similar to PTSD such as major depression(76). Baseline or resting studies generally have found no difference in plasma catecholamine levels between combat veterans with PTSD and normal controls. In contrast 24 hours urine studies have reported increased excretions of catecholamines and most challenge studies have found evidence of hyper responsivity of catecholamigic system(77). More research is needed for biological risk factors.

GENETIC

There is a significant genetic influence on symptoms liability even after adjusting for differences in combat exposure(78). Children of PTSD patients have higher risk of getting PTSD(79).

COMORBIDITY

Studies have found that PTSD seldom occurs alone(80-82). It can occur with work related impairment(83), Somatic complaints(84), substance abuse(85). Substances are initially used to modify the PTSD symptoms(86). With the development of dependence, physiological arousal resulting from substance withdrawal may increase PTSD symptoms, thereby contributing to relapse of substance use(86).

Among men with PTSD alcohol abuse or dependence was most common co occurring disorder followed by depression, anxiety disorder or other substance abuse other than alcohol(8,10). Among women co-morbid depression and other anxiety disorder preceded alcohol abuse and dependence(8,10). Other comorbid conditions include suicide(43,87) and social dys-functions (88,89) and somatization disorder (90).

TREATMENT

Use of pharmacological therapies have been described and almost all antidepressant have been tried for treatment of PTSD with some findings very good results. Evidence of the role of Serotonin in the modulation of HPA axis by means of modulation of CRF release comes from animal studies showing that long term administration of SSRI reduces the ex-pression of paraventricular nucleus CRP mRNA(91,92). Early trails with TCA found moderate positive efficacy for impramine and amitriptylin (93,94) and moderate positive for phenelzine(94). One study has given negative results for desimipramine(95). Fluoxitine was found to reduce the severity of PTSD symptoms by 40% after 5 weeks in one study(96) and improved 85% patients in another study(97). Paroxitine was found to reverse CRF alternations in stress associated with early maternal separation in primates (98). Doses of 20 and 40 mg of paroxtine were effective and well tolerated in treatment of chronic PTSD in all the three symptoms clusters of PTSD(99). Sertaline was found to be superior to placebo in reducing PTSD symptoms 53% versus 32%(100) FDA approved sertaline as the first drug for PTSD.

There is little evidence supporting use of benzodiazepines in PTSD and as many trails using these drugs were not successful(101,102). Research on the pharmacotherapy of PTSD began to increase in mid 1990 particularly spurred by pharmaceutical companies.

PSYCHOTHERAPY

Psychotherapy can be integrated with pharmacotherapy or considered as a treatment alternative for patients with PTSD. Cognitive behavior therapy has been used successfully for the treatment of PTSD symptoms. Exposure treatment including flooding in imagination and flooding in vivo appear helpful(102-105).Prolonged exposure treatment and stress inoculation training are effective therapies for some patients with PTSD(106,107).

CONCLUSION

PTSD has a global significance and its impact in countries experiencing frequent disasters and social unrest for many years is likely to evolve as a huge public health concern .The costs to the individual as well as the society are substantial both in financial terms and in broader human terms.

The difference between PTSD and other psychiatric disorders is that by definition it follows the experiencing of a traumatic event characterized by horror and helplessness,. Biological dysfunction of the glutamanergic and GABA, amine neurotransmitters and neuro endocrine pathways possibly plays a fundamental part in the pathology. Some PTSD symptoms respond better to treatment than others. Long-term studies and appropriate measures of various dimensions of PTSD are required to assess the out come beyond short-term treatment results.

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INTRODUCTION

Winkelman[21] and Millard and Wolf[22] by which individual and isolated cells together with their processes are picked out.

Myelinated nerve fibres can be selectively stained by Weigert Pal technique, the principal of which depends upon the fact that after treatment with a suitable oxidizing agent (e.g. potassium dichromate), the myelin acts as a mordant towards the haematoxylin. The sections are first overstained with the haematoxylin and subsequently differnetiated. The stain is thereby removed from all tissues except the myelinated fibres which hold it tenaciously[23]. This method has a disadvantage in that it demonstrates only those fibres which are provided with myelin sheaths and since myelinated fibres may loose their sheaths some distance before they actually reach their destination, their precise termination cannot be demonstrated with certainty. Other simple and rapid methods for demonstration of myelinated nerve fibres are Weil's method[29] and solochrome cyanine technique[25,26].

With the introduction of electron microscopy (having high resolving power of 0.2nm compared to 200nm of light mocroscope) and the reliable embedding techniques, structural analyses of the nervous tissue has been revolutioned. Phase contrast microscopy has been used to study nerve cells and glia[27]. Interference and contrast interference microscopy have been used to assess the refractive index, concentration, water content and dry mass in living cells[28]. The confocal scanning laser microscope (CSLM) is a powerful tool for studying the morphology of complex fluorescent or reflecting structures, by its ability to perform optical sectioning of thick sections, and reconstruct 3-dimensional picture of these structures and with appropriate software provides images with high contrast and resolution[29,18].

2. NEURON TRACING TECHNIQUES

a) Degeneration of nerve fibres:

It is difficult to place small experimental lesions in a mass of nervous tissue but it is possible to cut axons alongwith their course and then study the process of degeneration and trace the neuron. The degenerated nerve fibres can be stained by various methods like Glees[20], Nauta and Gygox[30], Eager[31]. After axonal damage, we can trace the neuron because the neuronal soma is swelled up, nucleus is displaced to excentric position and nissl grannules degenerate (chromatolysis)[32]. When myelinated nerve fibre is damaged, the myeline sheath distal to the lesion undergoes degeneration (Wallerian degeneration)[4] which can be stained by Marchi technique (modified by Swank and Davenport)[33,34].

b) Autoradiography, which locates radioactive material (like tritiated leucine) in sections of biological tissues, can be used to trace the course and termination of neural tracts like optic tract [35,36].

c) Stereotaxis and selective lesions:

In stereotaxis, the head of an experimental animal is fixed in a rigid frame in which an electrode or micropipette can be adjusted in three planes to previously established coordinates and thus aligned with a target within the brain[37]. Previously steriotactically placed focal lesions have been produced using fine electrode, probes (which produce intense cold at their tips), implants of destructive substances such as alcohol, hydrocyanide, carbon dioxide snow, radioactive yttrium, focussed ultrasound or proton beams. Ribosome inactivating protein, has been used to achieve greater selectivity in two ways: Suicide transport and Immunolesioning. Suicide transport technique depends upon the axonal uptake and transport to neuronal perikarya of cytotoxic lectins such as ricin, abrin, viscumin, vilkensin and produces the selective death of neurons. In immunolesoning, monoclonal antineuronal antibodies conjugated to various toxin moieties have been used to knock out specific groups of neurons[38].

3. IMMUNOHISTOCHEMISTRY

Immunohistochemical methods involve the production and identification of site of antibody-antigen interaction in tissue sections. At present, immunolabelling techniques are the most reliable means for identifying neural structures. Also, immunohistochemical techniques provide more consistent staining of neural tissues than the classical gold, silver and methylene blue methods[39]. Immunolabelling techniques utilise fluorescent markers like fluorescein isothiocynate, rhodamine, horseradish peroxidase, colloidal gold, protein gene product 9.5, substances P (Protein S) calcitonin gene related peptide, neurofilament, vasoactive intestinal peptide etc. [18,40,41]. Histochemical techniques use either the pre-embedding labelling technique or post embedding technique. In pre-embedding technique, many antigens are lost or denatured at sites of low concentration. So, post-embedding techniques are used for electron microscopy, in which the tissue is fixed, embedded and sectioned and the immunolabelled[42]. Post embedding technique may further be improved by use of progressive lowering of temperature combined with UV-polymerization of a methacrylate based resin. These newer methods have not only been used to study the neural structure but have also been used to study reinnervation of denerved tissue, either by collateral sprouting from intact neighbouring nerves or by expansive regeneration[40,43,44].

4. TISSUE CULTURE

The technique of tissue culture consists in placing a minute fragment of fresh tissue in a suitable nutrient medium and preserving it (under asceptic conditions under suitable temperature) in a sealed chamber on a microscope slide or in a watch glass, flask, or some other glass receptacle which enables it to be examined microscopically. The technique of tissue culture was originally given by American anatomist R.G. Harrison in 1907 while he was studying the origin and growth of nerve fibres. He found that nerve fibres grow out directly from explanted neural tubes and proved that axons were derived from neurons and were not composed of independent units[45,46]. Experimental manipulation of selected populations of cells in tissue culture has provided valuable insights into many aspects of neural function including regulatory factors affecting glial and neuronal development, the mechanism of myelination and demyelination etc[47].

5. NEURAL TRANSPLANTATION TECHNIQUES

Numerous studies have shown that transplants of fetal central nervous system tissue into preformed cavities within a host brain can become functionally integrated with the host tissue and the transplanted cells may take part in the function of host tissue[48]. It is also now known that injury to nervous system causes vigorous formation of new synapses by surviving axons[49]. Embryonic neurons (in experimental mice) survive transplantation into adult hosts and both give and receive normal patterns of specific functional synaptic connections which integrate them into the host brain[50]. In some degenerative conditions, like Parkinson's diseases fairly specific category of neurons are lost and attempts have been made to replace the lost cells by injections of embryonic neurons of similar type to ameliorate the symptoms. But where tracts are involved, as in stroke affecting the internal capsule, a comparable regenerative response may be obtained by implantation of peripheral nerve segments as bridges, but even in best conditions, only a minor proportion of the cut axons are able to regenerate[56].

An ability to propagate pluripotent embryonic cells (stem cells) in culture is the foundation both for defined germline modification in experimental rodents and for future possibilities for broad based cellular transplantation therapies in humans[52]. Mouse embryonic stem cells can be induced to differentiate into neurons and glia when cultured in presence of retinoic acid[53]. Transplantation of neurons and neural precursors is currently an active area of research[54,55].

From the above account, it is clear that neural culture and transplantation are still in experimental stage, whileas immunohistochemistry has gone a long way in interpretation of nervous structure. The conventional tissue staining methods (like silver impregenration) are still widely used to understand basic neural organisation; immunohistochemistry alongwith scanning electron microscopy is used to study the nervous structure, in relation to its function, in depth.

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CLINICAL VALUE OF FINE NEEDLE ASPIRATION CYTOLOGY AND BIOPSY IN THE EVALUATION OF MALE INFERTILITY

...A comparative study of 60 infertile patients

Mufti Mahmood, Jagdishwar Kumar Singh, U.S. Dwivedi, Mohan Kumar, P.B. Singh

ABSTRACT

To compare the diagnostic value of cytological smears of fine needle aspirate with that of histological sections obtained by testicular biopsy in the evaluation of infertility, 60 patients of infertility with azoospermia and severe oligospermia (sperm counts of <5 million/ml) were undertaken for the study. A detailed history was taken and the duration and type of infertility whether primary or secondary was noted. A thorough general physical examination included the examination of the genitalia. Testicular samples were obtained by fine-needle aspiration using a 10 ml syringe and 21-gauze needle. The samples were fixed in 95% alcohol and stained with papanicoloau stain. A testicular biopsy was taken after exploring the same tract and these sections were stained with haematoxylin and eosin. The cytological smears and histological sections were examined separately and the results compared. The cytological smears were divided into four groups: normal, with all spermatogenic cells present, hypospermatogenesis; spermatogenic arrest and sertoli cell only syndrome. There was 95% correlation between the diagnosis on the cytological smears and histological sections. However, there was some discrepancy in hypospermatogenesis and maturation arrest groups, they being difficult to diagnose even on histology.

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INTRODUCTION

Infertility is defined as one year of unprotected coitus without conception as proposed by the American Fertility Society[1,2]. Approximately, 15% of couples are unable to conceive a child after one year of regular unprotected intercourse. A male factor is solely responsible in about 20% of infertile couples and contributory in another 30-40%.[3] The evaluation of spermatogenic function by testicular biopsy is especially important in patients with fertility compromised by obstructive azoospermia. Testicular biopsy was first described by Charney[4] and was used clinically by Hotchkiss.[2] Persson et al[5] performed fine-needle aspiration (FNA) of the testis in 42 patients with azoospermia and popularized the method. Compared with testicular biopsy, which is more invasive and painful, and requires theatre facilities, FNA is more rapid and minimally invasive.

In this study, we compared the results of cytological smears obtained by FNA with those from histological sections of testicular biopsy specimens.

MATERIAL AND METHODS

This prospective study was conducted on 60 patients of azoospermia and severe oligospermia who were assessed in the Department of Urology, Institute of Medical Sciences, Banaras Hindu University, Varanasi from June 1999 to 2002. A detailed history was taken and the external genitalia examined to evaluate the possible causes of infertility. The urogenital examination included the site and presence of the testis and condition of the penis. The testicular volume was measured by Prader orchidometer; both the epididymes and vasa were palpated for any abnormalities; a DRE was carried out to exclude prostatitis and dilated seminal vesicles. Two semen samples were analysed in all patients and their serum FSH levels evaluated. All patients were then subjected to FNA and testicular biopsy of the same testis. The FNA was performed under local anesthetic,

Key words: Infertility, testis, fine-needle aspiration cytology, azoospermia.

infiltrated into the cord structures. The testis was aspirated at three separate sites using a 21G needle and 10 ml syringe. The samples were then wet fixed in 95% alcohol and stained with papanicoloau stain. After FNA, incision was made over the puncture sites of the testis to explore the tract. A 5 mm specimen of the testis was excised, fixed in Bouins fluid, embedded in paraffin, cut into 4 mm sections and the sections stained with haematoxylin and eosin (H & E). The cytological smear and histological sections were examined separately and the diagnosis compared.

Cytologically there are two different cell populations:

1. Sertoli cells
2. Cells in various stages of spermatogenesis

Sertoli cells have a round, vesicular nucleus which shows finely granular chromatin and usually contain a large nucleolus. The cytoplasm is abundant, pale and vacuolated, with poorly delineated borders. The various spermatogenic cells are spermatogonia, primary spermatocytes, secondary spermatocytes, spermatids and spermatozoa. The spermatogonia are usually uninucleate but occasionally are binucleate or with multinucleate. Primary spermatocytes have a large nucleus with thread-like or coarse chromatin. Secondary spermatocytes are rarely identified because of their short life span and immediate transformation into spermatids. Spermatids have a much smaller nucleus than the spermatocytes, corresponding to their haploid set of chromosomes. Spermatozoa have oval nuclei with very dense chromatin. The tail is formed on the opposite side of the acrosome.

Depending on the type of cells present in the cytological smears, they were classified into four groups: normal (all the common cells of spermatogenesis, including spermatogonia, primary and secondary spermatocytes, spermatids, spermatozoa and sertoli cells present); Hypospermatogenesis (quantitative reduction of the cells of spermatogenic line along with normal pattern of sertoli cells); Maturation arrest (higher proportion of immature cells with absence of mature spermatozoa); Sertolic cell only (only sertoli cells with total absence of the spermatogenic cells).

RESULTS

Of the 60 patients, 56 (93%) patients had primary infertility while 4 (7%) patients had secondary infertility. 4 (7%) patients had left sided varicocele with bilateral normal tests. 1 (2%) patient had bilateral maldescended testes which were located in the superficial inguinal pouch. 34 (57%) patients had normal sized testes and 26 (43%) had bilateral small sized testes. 46 (77%) patients were azoospermic and 14 (23%) patients were oligospermic. Estimation of serum FSH levels of 46 asoospermic patients revealed normal levels in 32 (70%) patients and raised levels in 14 (30%) patients. Overall, out of 60 patients 57 (95%) patients showed complete agreement between the cytological smears from FNA and the histological sections obtained y biopsy (Table I)

Few significant complications occurred after FNA compared with biopsy, with pain in 12 and haematoma in 7 patients. After biopsy, 17 patients had pain and 12 hematoma with 31 having scarring and 8 having infection at the incision site.

Table I: COMPARISON OF CYTOLOGICAL SMEARS FROM FNA AND HISTOLOGICAL SECTIONS FROM TESTICULAR BIOPSY

		Histopathological Diagnosis				
Cytological diagnosis	No. of patients	Normal spermato-genesis	Hyposper-matogenesis	Maturation arrest	Sertoli cell only synd.	Testicular atrophy
		I	II	III	IVA	IVB
Normal spermatogenesis	36	36	-	-	-	-
Hypospermatogenesis	6	1	5	-	-	-
Maturation arrest	10	-	1	8	-	1
Germ cell depopulation	8	-	-	-	6	2
Total	**60**	**37**	**6**	**8**	**6**	**3**

Table II: LITERATURE ON CORRELATION BETWEEN FNA AND BIOPSY

Study	No. of patients	% Agreement
Person[6]	42	86%
Gottschalk-Sabag[10]	47	87%
Mallidis[11]	46	94%
Craft[6]	19	84%
Odabas[8]	24	90%
Mahajan[7]	60	97%

DISCUSSION

Since its description in 1965, the use of testis FNA in the diagnostic algorithm of male infertility has been studied extensively.[3-6] Some studies have examined the ability of testis FNA to define testis histology and other spermatogenic pathology, and others have outlined the detailed cytologic characteristics of the seminiferous epithelium in the correlation rates of cytologic and histologic interpretation of testis pathology found in prior studies that have compared FNA with biopsy. In general, these studies demonstrate high rates of correlation (Table II). We observed a correlation of 95% in our study.

Despite similar high correlation rates in this and other comparative studies of cytology and histology in male infertility, one major difference is evident. The methodology presented in many prior studies is difficult to translate effectively into routine clinical care becaue of the complexity of the cytologic assessment.[9,13,15] Some authors have addressed the problem of classifying testicular cytology with a quantitative analysis of the spermatogenic cell to the sertoli cell.[9,13] More recently, Batra et al[15] found that individual cell counts and indices found on cytology correlated well with histology. Although all of these methods may be accurate, they are time and labor intensive.

In establishing diagnosis from FNA cytology, we used the concept of pattern recognition. Specifically this involves the assessment of three fairly easily indentified germ cell types: primary spermatocyte, spermatid and spermatozoa. Exact cell numbers were not quantified, but their allowance was assessed relative to the cytologic findings in case of normal spermatogenesis. Our system is similar to that of Gottschalk Sabag et al[10] in the general patterns of spermatogenic cell types. The excellent agreement of cytologic and histologic readings suggest that this method may hold future promise as an interpretive technique.

The findings of histologic variation within the infertile testis has tremendous clinical implication, given the advances in assisted reproductive technology. This is no better exemplified than the cases of biopsy histologic exhibiting a sertoli cell only pattern. Despite a diagnostic histologic finding of complete lack of germ cells within the seminiferous tubules, clinical experience in men undergoing testicular sperm extraction and intracytoplaskic sperm injection have demonstrated that testes with this histologic can harbor useable sperm and that pregnancies can be achieved.[16-18]

This simple fact suggests that diagnostic techniques that allow for multiple samplings of testis tissue, such as FNA mapping, may have better potential to discriminate those men with potential to discriminate those men with pockets of sperm production despite a diagnostic biopsy that suggests otherwise.

Limitations to testicular FNA cytology include an inability to assess the status of the tubular basement membrane. Basement membrane thickening is a common histologic observation in states of fibrosis and atrophy, but is not evaluable by cytology. In cases of infertility, information about the basement membrane does not alter clinical care if the status of spermatogenesis is clear.

In conclusion the high correlation between biopsy histology and FNA cytologic findings in this study suggest that an evaluation of formal cellular architecture of testis is not necessary to diagnose various states of spermatogenesis.

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EXTERNAL FIXATION AND DELAYED UNREAMED INTRAMEDULLARY INTERLOCKING NAILING OF OPEN FRACTURES OF TIBIA. (A PROTOCOL).

Suhail Afzal, Mohd.Ramzan Mir, Munir Farooq, Nazir A Wani, Shabir A Dhar, Sajad Moulvi, Fayaz A.Dar, Asif Sultan.

ABSTRACT:

Between June 2001 and Aug 2003, 27 open fractures of the Tibial shaft were treated with debridement and provisional external fixation, followed by delayed soft closure and subsequent interlocking nailing without reaming. There were 11(39%) grade-I fractures and 17(61%) grade-II fractures. All the fractures were the result of road traffic accident. The average duration of external fixation was 3weeks.The average time between removal of the fixator and intramedullary nailing was about 2 weeks. Mean time to union was 29 weeks for grade 1 fractures and 32 weeks for grade 2 fractures. There were 2 infections(7%) at the site of grade2 fractures. Both infections healed, with retention of nail and without chronic osteomyelitis. There was one Non union and two delayed unions. This sequential protocol for treatment, which involved a short period of external fixation and delayed intramedullary interlocking nailing thus minimized colonization of the pin tracks, is a simple and effective technique with good results and a low rate of infection, in treating these fractures.

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A tibial shaft fracture is a common injury largely owing to its superficial location and the subcutaneous characteristics of its anteromedial aspect easily cause open fractures[1,2]. For open fractures of the tibia, external fixation is the most widely used technique[3,4]. It not only provides stability of the fracture fragments but also permits local soft tissue management. The eccentric position of the tibia can maintain a longer period of pin insertion[5], and patients can ambulate with such a framework. However despite many refinements in this technique, it has been associated with numerous complications, including problems at the sites of the pins, non union, delayed union, malunion and infection [4-7]. Alternative methods of management, include primary internal fixation with intramedullary nails[8-10]. The biomechanical and biological advantages of intramedullary fixation of closed fractures of the tibial shaft have been reflected in excellent clinical results[11-14]. The primary use of the nails for fixation of open fractures of the tibia is very controversial because of the risk of infection. Delayed insertion of intramedullary nails after a period of external fixation has been mentioned in several reports of open tibial fractures[11,15,16,17,18]. The locking of intramedullary nails to the major proximal and distal fragments decreases the prevalence of the malunion of fractures. Until recently, however, all interlocking nailing involved reaming, which destroys the endosteal blood supply[18,19]. The rate of infection after treatment of open tibial fractures with intramedullary nailing with reaming has been relatively high, causing most of the investigators to discourage the use of this technique for open tibial fractures[20,21]. At our institution, a sequential protocol consisting of debridement, external fixation, closure of the wounds and intramedullary interlocking nailing without reaming has been used for selected patients who had open tibial fractures.

MATERIALS AND METHODS:

Between June 2001 and Aug 2003. twenty eight consecutive Type1 and Type2 open fractures were treated with unreaned interlocking nailing after debridement and provisional external fixation at our institution. Patients were aged from 19-57 years(average 32 years) with a male to

Key Words: Open tibial fractures, External fixators, unreamed interlocking nailing.

female ratio of 3:1. Most of the fractures were caused by road traffic accidents. The soft tissue injuries were classified according to the sustem of Gustillo et al. Eleven wounds were grade-1 and 17 were grade-2. The comminution of the fracture was graded according to the scale of Winquist et al. Fourteen had grade-1 comminution, ten had grade-2 comminution and four had grade-3 comminution. The initial management was started at the emergency service. After stabilizing the patients, open fractures were debrided and immediately fixed with external fixation in the operation room. Emergency operation was done with a goal of thorough debridement of the wound within six hours of injury. However, this was frequently not possible due to the referral nature of our practice which serves a larger area. The average time from the injury to the debridement was 7.4 hours. Eight fractures were debrided more than nine hours after the injury. The site of the wound was thoroughly excised,debrided and irrigated and external fixator was applied. Early in the course of the study, a number of delta configuration frames were used, but we now recommend the use of a uniplanar frame only. The wound was left open and was repeatedly debrided as necessary. The wounds were dressed with a sterile dressing and all the patients received intravenous antibiotics. The right leg was involved in fifteen patients and the left leg in thirteen patients. Twelve fractures involved the middle of the tibial shaft, eight in the junction between the proximal and middle thirds, six in the junction between the middle and distal thirds and two the distal thirds. An attempt was made to obtain soft tissue closure by the fifth to seventh day. When the wound had healed satisfactorily, the external fixator was removed and the limb placed in a splint or if the fracture was grossly unstable, in calcaneal traction. The sites of the pins and the wounds were monitored for an additional week. When they were dry and if there was no infection, closed intramedullary interlocking nailing without reaming was performed. A fracture table was used for insertion of the nails. Standard tibial nails were used for all the fractures. A calcaneal pin was used for traction. The hip was flexed 45 degrees and the knee was flexed 90 degrees. Image intensification was used to ensure that the tibia was restored to its proper length, and the fracture was reduced before nailing was begun. The limb was then prepared and draped. A longitudinal incision was made medial to the patellar tendon and the tendon was retracted laterally. A curved awl was used to make the entry point at the midline of the tibia at the level of the fibular head. A nail of the proper length and diameter was inserted over the guide wire with the help of an insertion jig. Once the nail was properly seated, the guide wire was removed. The proximal locking screws were placed medial to lateral with the use of insertion jig and image intensifier. The distal locking screws were placed from medial to lateral with a free hand technique guided by image intensifier. Two proximal and two distal locking screws were used in all. In this series fourteen, eight millimetre nails, eight, nine millimetre nails and six, ten millimetre nails were used. It is our policy to lock all nails statically. Post operatively patients received cephalosporin and an aminoglycoside. After the nailing rehabilitation included mobilization of the adjacent joints as soon as possible. The time to weight bearing varied according to the fracture pattern. Unless it was contraindicated weight bearing was permitted for all the patients within six weeks after the nailing. Secondary bone grafting was done for the fractures with more than 50% comminution and in one case which was a non union. Dynamization was done in three patients ,one of non union and two of delayed union. Patients were scheduled for follow up visits at monthly intervals.

The external fixator was removed at an average of 21 days after injury. Intramedullary nailing was performed at an average of two weeks after removal of the fixator. For the patients who had an isolated injury, the stay in the hospital averaged 30 days(11-55days).

RESULTS:

Union: was defined as the presence of bridging callus on the radiographic views and the ability of the patient to bear full weight on the injured extremity. All of the 28 fractures united. The time to union averaged 29 weeks for grade-1 fractures and 32 weeks for grade-2 fractures. One non union occurred in a patient of grade 2 fracture and Winquist grade 3 comminution , which needed bone grafting and dynamization. Two of the delayed unions healed satisfactorily after dynamization.

Range of Motion: The flexion arc of knee averaged 139 degrees. The range of motion of the ankle averaged 16 degrees of dorsiflexion and 38 degrees of plantar flexion.

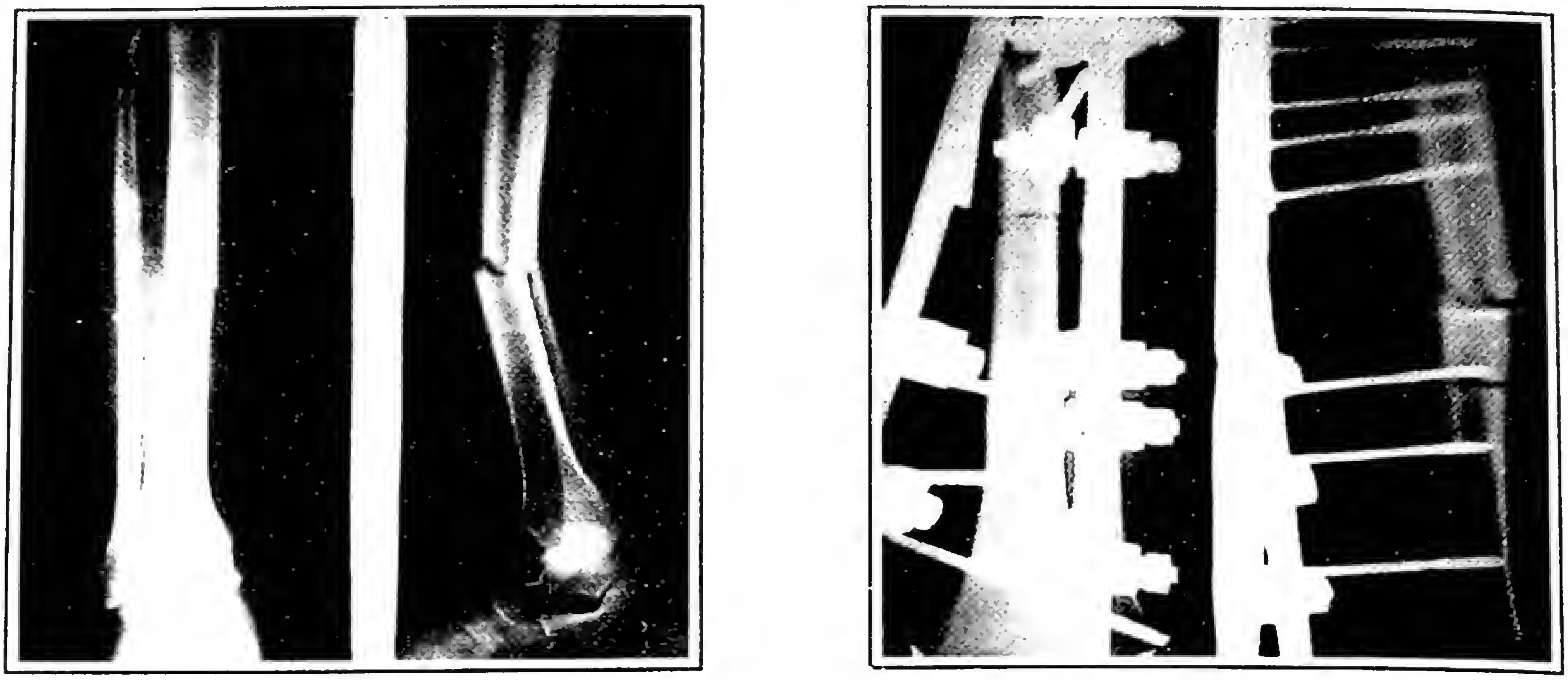
Malunion and Malrotation: Malunion was defined as varus or valgus angulation of more than 5degrees, Anteroposterior angulation of more than 10 degrees or shortening of more than 1 centimeter. Malrotation was evaluated by comparing the amount of internal and external rotation of the injured extremity with those of the normal extremity. There were no rotational deformities.

Infection: There was infection at the sites of two grade 2 open fractures. Both the patients were treated with antibiotics, sterile dressings and repeated debridements. No active infection was evident in any of the patients at the time of the most recent follow up.

DISCUSSION:

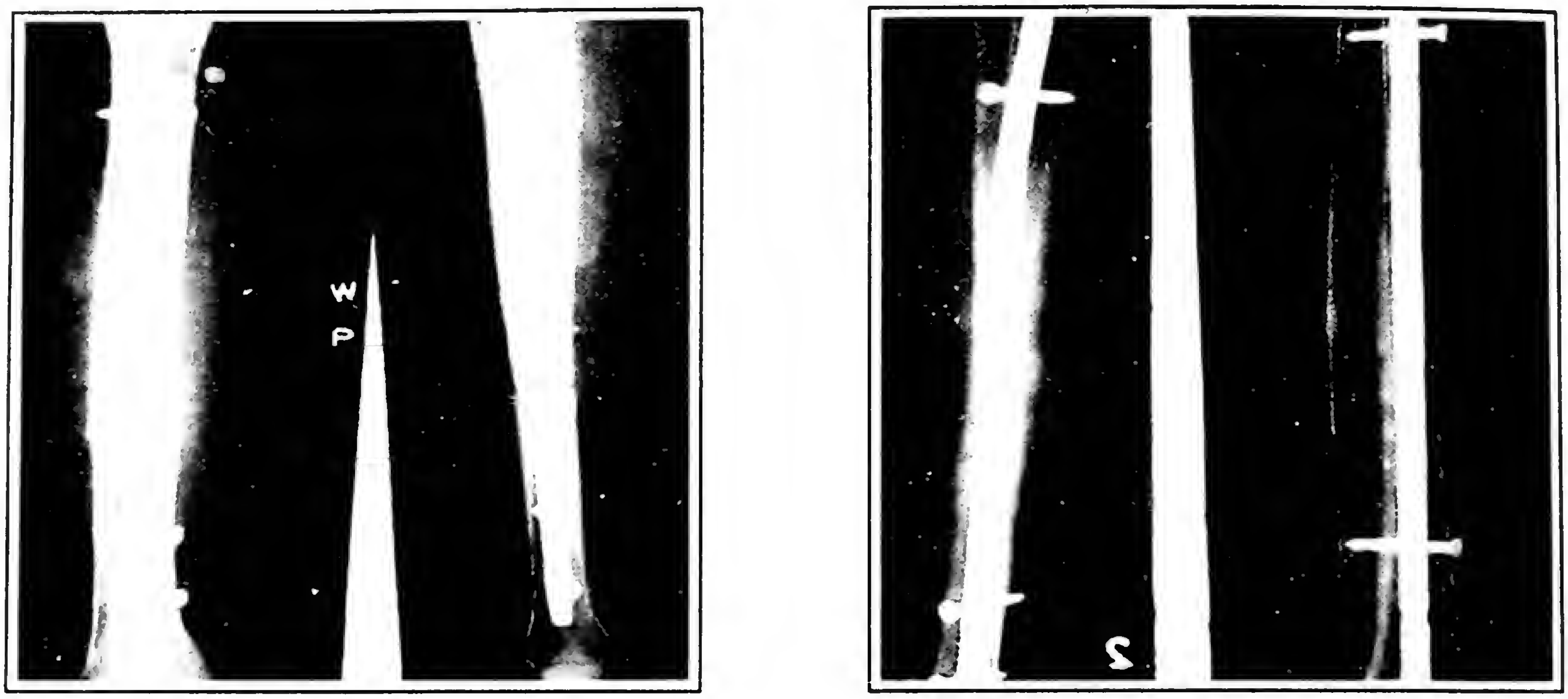
Open fractures of the tibial shaft have always been complicated by problems of maiunion,non-union and infection,sometimes resulting in amputation. The excellent results in our series of patients corroborate the effectiveness of this sequential treatment of open tibial fractures. If the wound is debrided thoroughly,closed expeditiously and the external fixator is removed early, the benefits of intramedullary interlocking nailing without reaming can be obtained without an unacceptably high incidence of infection. A study of larger series of open fractures is needed to confirm the efficacy of this treatment for severe open fractures of the tibia.

X-RAY OF A PATIENT WITH TYPE - II OPEN FRACTURE OF TIBLA



Pre-Op

On external fixator



Post-Op

(Unreamed I.L. Nail)

Final follow up

(# United)

In 1975,Karlstrom and Olerud[4],were the first to mention intramedullary nailing after external fixation. They reported on a single patient who had a three month old fracture, the treatment of which was complicated by deep sepsis. Clancey[9] and Velazco et el[10] reported on two and five patients respectively.All of these patients had a delayed union, but the results were not elaborated on. Interlocking intramedullary with reaming solves the problem of malunion because it provides the ability to control length, rotation and infection. Reaming however, destroys the endosteal blood supply, further devascularizing already compromised bone[19].

Intramedullary nailing without reaming is less damaging to the endosteal blood supply than is nailing with reaming and historically it has resulted in lower rates of infection. To our knowledge McGraw and Lin,reported the earliest study that dealt specifically with nailing after external fixation.In only nine of their sixteen patients was nailing done as part of the orginal plan of treatment. The average time to nailing was seven weeks. The rate of infection was 44% and the rate of non union was 50%. Another such study by Piotr A[17] reported 5% infection rate in 39 patients with two non unions and one delayed union. Peige A et al[18] in another study reported 8% infection rate in fifty open fractures with overall good results. We found that a protocol of early delayed nailing(average of 21 days of external fixation) gave excellent results, without a high rate of infection. Function was restored rapidly and many of the complications of external fixation were avoided. The disadvantages of the technique are the need for several operative procedures and a longer period of stay in hospital.

CONCLUSION:

Our experience as well as that of others[13,17,18,20,21,22] suggests that treatment of low grade open fractures of the tibia by delayed undreamed intramedullary interlocking nailing of the tibia yields excellent results. The sequential treatment used in this study provided a satisfactory alternative for the treatment of open fractures of tibia.

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ADVERSE EFFECT PROFILE OF STREPTOKINASE THERAPY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: A PROSPECTIVE STUDY.

Javid A Malik, G.Q. Khan

ABSTRACT

Active surveillance of adverse reactions to already marketed drugs must continue for the whole life span of the drug. Streptokinase (SK) is an extensively used thrombolytic agent for the management of patients with acute myocardial infarction (AMI). We conducted a prospective evaluation of the adverse effect profile of SK.

All patients admitted to the Cardiology Unit of Govt. Medical College hospital Srinagar, India with a diagnosis of AMI were eligible to participate in the study if they did not have any of the exclusion criteria. Eligible patients received 1.5 million units of streptokinase intravenously in normal saline over 1 hour. Blood samples were drawn for various hematological and biochemical investigations. Patients were meticulously monitored for all possible adverse effects, if any.

Out of 163 patients of AMI, 102 (62.5%) were thrombolysed. The two most common contraindications for thrombolysis were sustained B.P > 180/110 and presentation later than 12 hours. Thrombolysis was successful in 47% patients. Bleeding from various sites occurred in 11(10.7%) patients including 4 cases of upper gastrointestinal bleed and 2 cases of macroscopic haematuria. Hypotension and minor allergic reactions each occurred in 6 (5.8 %) patients. We observed few unusual complications of streptokinase therapy like thrombocytopenia in 3 patients, subnephrotic proteinuria in 2, and non-oliguric acute renal failure(ARF) in one patient. Both thrombocytopenia and ARF were self-limited.

Conclusion: Streptokinase is a relatively safe drug with modest efficacy and has low incidence of life threatening adverse effects. Therefore its use should be encouraged whenever indicated in acute myocardial infarction, especially when primary PTCA is not available.

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INTRODUCTION

Streptokinase (SK) is an enzyme derived from certain strains of β-hemolytic streptocci.1 It consists of a single polypeptide chain with a molecular weight of 47,000 daltons and contains 414 amino acids.2 Isolated in 1953, it was the first thrombolytic drug to be used and is the most widely prescribed and least expensive of the drugs used.[1,3] It is usually administrated intravascularly to treat a wide range of diseases associated with pathological activation of haemostasis like acute myocardial infarction (AMI), pulmonary thromboembolism, deep vein thrombosis (DVT) and acute arterial occlusion. It is however in AMI that its use has been most widely studied with several large multicentric trials showing efficacy of thrombolytic therapy in general and of streptokinase in particular.[4-6]

Being a foreign protein, SK is antigenic and is responsible for a variety of allergic reactions, including rash, hypotension, and serious anaphylactic reactions (urticaria, bronchospasm, angioedema).[7] The most common complication of SK therapy is bleeding and the most catastrophic complication is intracranial haemorrhage (ICH) which has an incidence of approximately 0.1-0.5%.[8]

Despite the easy availability and extensive use of SK in India, to the best of our knowledge, a prospective evaluation of its adverse effect profile in patients with AMI has not been done.

Key words: Streptokinase, Adverse effects, Thrombolysis, Acute myocardial infarction.

Therefore, the present study was conducted with the main aim of evaluating the adverse effects associated with SK therapy.

The study was conducted in the Cardiology Unit of the Government Medical College Hospital, Srinagar, India. This is a 500-bed tertiary care hospital catering mainly the population of the state of Jammu & Kashmir. All patients admitted into the Cardiology Unit with a diagnosis of AMI were eligible to participate in this prospective study if they received thrombolysis with SK in the hospital.

AMI was diagnosed if two or more of the following were present : sudden development of prolonged (>30 minutes) anterior chest discomfort, electrocardiographically detected ST-segment elevation in two contiguous leads of at least 2mm, elevation of cardiac enzymes (CK-MB, troponin T) and appearance of segmental wall motion abnormality on echocardiography.

The study was conducted between March, 2001 and April 2002. During this period 163 patients of AMI were admitted, out of whom 102 (62.5%) were thrombolysed using 1.5 million units of SK in normal saline over one hour. Sixty one patients were excluded from the study; the reasons for exclusion are given in Table 1.

Disappearance of chest pain and resolution of ST segment elevation by two-thirds at 90 minutes post-thrombolysis with or without reperfusion arrhythmias were considered as indicators of successful thrombolysis. Patients who had reperfusion failure were referred for rescue percutaneous coronary intervention (PCI) to appropriate centers.

All those patients who received SK also received low molecular weight heparin (LMWH) for the next five days in addition to aspirin, angiotensin converting enzyme (ACE) inhibitors, â-blockers and statins. Blood samples were drawn for complete blood count (CBC), blood sugar, serum creatinine, CPK, AST, LDH, and lipid profile. Urine analysis and 24 hour urinary protein were ordered in all patients as was Troponin T. Patients were monitored for mechanical, electrical and fibrinolytic complications and further investigations and management was accordingly planned. Previous medical records wherever available were thoroughly reviewed. Upper GI endoscopy was done 1 month after discharge in 4 patients who developed gastrointestinal bleeds.

RESULTS

Baseline characteristics of all patients are given in table 2: Out of the 102 patients of AMI who received SK, 29 (28.4%) developed complications related to this drug (Table 3). Overall the adverse effects were more common in males as compared to females (62% vs 38%).

The commonest complication observed was bleeding from various sites that occurred in 11 (10.7%) patients (Table 3). Bleeding from vascular puncture sites and gastrointestinal tract each of which occurred in 4 (3.9 %) patients were the two most common sites followed by macroscopic haematuria 2 (1.9%) and a big haematoma into the medial aspect of the right thigh of a 70 year old diabetic female (Table 4). None of our patients developed ICH and there was no death directly related to SK thrombolysis. All the 4 patients who developed upper GI bleed were males, had a mean drop in haemoglobin of 4 g/dL and all of them needed blood transfusion. Upper GI endoscopy done one month after discharge from hospital was normal in all these 4 patients.

Table -1

REASONS FOR EXCLUSION OF PATIENTS FROM THE STUDY.

1. Sustained BP > 180/110 at presentation.
2. Past history of intracranial haemorrhage at anytime or non- haemorrhagic stroke within one year.
3. Known intracranial neoplasm.
4. Active internal bleeding (excluding menses)
5. Patient on oral anticoagulants with an INR > 2.5 and patients with known bleeding diathesis.
6. Active peptic ulcer and gastrointestinal bleeding in preceding 1 month.
7. Suspected aortic dissection.
8. Recent major surgery (< 3 wks)
9. Pregnancy
10. Streptokinase related thrombolysis (5 days to 2 years) or significant hypersensitivity reaction.
11. Acute pericarditis.
12. Late presentation (i.e. more than 12 hours from the onset of symptoms)

Table 2

Baseline characteristics of the study patients (n=102)

Total No of AMI patients= 163 (M=109,F=54)
No of patients thrombolysed =102 (62.5%)
Troponin T positive =158(96.9%)
Elevated CPK=146(89.5%)
Successful thrombolysis =48(47%)

Characteristics of AMI patients	Male	Female
Total (thrombolysed) Number (%)	58(57)	44(43)
Age (years)		
Mean (SD)	46(15)	51(13)
Range	32-78	44-76
Risk factor No. (%)		
CAD	41(40)	37(36)
Hypertension	20(19)	18(17)
Diabetes	15(14)	20(19)
Dyslipidemia	14(13)	11(10)
Smoking	45(44)	11(10)
Family history of CAD	30(29)	34(33)
No. of drugs receiving at admission, mean (SD)	3.2(1.4)	3.1(1.6)

Table 3

ADVERSE EFFECTS OBSERVED IN STREPTOKINASE RECIPIENTS:

Complications	No.(%)* of patients	Mean Age (Years)	Male. No. (%)**	Female No. (%)**
1 Bleeding from various sites	11(10.7%)	53	8(73)	3(27)
2 Hypotension	6(5.8%)	52	3(50)	3(50)
3 Allergic reactions	6(5.8%)	54	4(67)	2(33)
4 Thrombocytopenia	3(2.9%)	46	2(67)	1(33)
5 Proteinuria	2(1.9%)	62	0(0)	2(100)
6 Acute renal failure	1(0.9%)	47	1(100)	0(0)
7 Intracranial haemorrhage	Zero	–	–	–
8 Deaths directly related to SK	Zero	–	–	–
Overall	29 (28.4%)	52	18 (62%)	11 (38%)

* % denotes percent of all patients.

** % denotes percent of patients with that particular adverse effect

The second most common complication was hypotension that affected six (5.8%) patients including 3 males and 3 females who had a mean age of 52 years. It responded to reduction in the rate of SK infusion and 200 mg of intravenous hydrocortisone. Transient thrombocytopenia occurred in 3 (2.9%) of SK recipients — all were relatively young (mean age 46 years) and their mean platelet count was 60,000. Other cell lines were unaffected and platelet count normalized within 2 weeks.

Renal involvement in the form of subnephrotic proteinuria occurred in two female patients and non-oliguric acute renal failure (ARF) occurred in one patient. All the 3 patients had recently documented normal kidney function tests before they developed acute coronary syndrome. They were all non-diabetic, had no history of nephrotoxic drug intake and their collagen vascular disease profile was negative. A 47 year old male who received SK within two hours of onset of chest pain and who's BP remained normal throughout the hospital course developed non- oliguric ARF on the second day of AMI. He did not need any dialysis and regained normal kidney function tests within 10 days of hospitalization. However the other two patients continued to have non-progressive subnephrotic proteinuria till the last out-patient follow up (3 months). Renal biopsy was planned if proteinuria persisted beyond six months. Thrombolysis was considered successful in 48 (47%) patients based on subsidence of chest pain and resolution of ST segment elevation by at least two-thirds at 90 minutes post-thrombolysis.

DISCUSSION

A collaborative overview of placebo-controlled trials of intravenous thrombolytic therapy, encompassing more the 60,000 patients has clearly shown that thrombolytic therapy is effective in all patients with AMI admitted to hospital within 12 hours of the onset of symptoms.[5]

The present study involved 102 patients of AMI who received SK (1.5 million units) within 12 hours of onset of chest pain. Successful reperfusion was achieved in 47 % patients who received this drug. A quantitative scale known as Thrombolysis in Myocardial Infarction (TIMI) grading system that assesses the flow in the culprit artery (grade 3 flow being the goal of thrombolytic therapy) could not be applied since coronary angiography was not possible in our hospital. Coronary recanalization rates of 40-45% with SK and 65-70% with r-tPA, (a more costly drug), are known. We observed SK related complications in 28.4% but no deaths directly related to it. The commonest complication (10.7%) that we encountered was bleeding from various sites including vascular puncture sites, gastrointestinal mucosa, haematuria and skeletal muscle. Bleeding is known to be the most common complication of SK therapy. Minor bleeding (not requiring transfusion) occurs in 3 to 4% of patients in the absence of invasive procedures.[8,10]

Various series have reported that 70% of bleeding episodes occur at the sites of vascular punctures and microscopic hematuria and blood streaked sputum or vomitus are also noted. Significant or major bleeding (requiring transfusion) occurs in approximately 1% of patients.[8] Intracranial haemorrhage (ICH), the frequency of which varies with the clinical characteristics of the patients and the thrombolytic agent used, is the most dangerous complication of thrombolytic therapy occurring at an incidence of 0.1 to 0.5%.[13-15] In the present study, no such complication was observed.

Table 4

PATIENTS WITH BLEEDING COMPLICATIONS

Site of bleeding	No. (%) of patients*	Age (mean)	Sex (M:F)	Mean Hb drop G/dL	Transfusion required, if any
Vascular punctures	4(3.8%)	50	2:2		-
Upper GI tract	4(3.9%)	65	4:0	4	2-4 units
Urinary tract	2(1.9%)	55	2:0	2	-
Muscles and skin	1(0.9%)	70	0:1	1	-
Intracranial	Zero				

* % denotes percent of all patients.

Transient hypotension is caused by SK in many patients, but significant allergic phenomena like bronchospasm, rash and serum sickness-like illness occur in only minority of its recipients. 16 In our series 5.8% patients developed hypotension that responded to slowed rate of SK infusion and a bolus dose of short acting steroid.

Three relatively young patients developed thrombocytopenia with a mean platelet count of 60,000 that resolved within 2 weeks without any treatment. Thrombocytopenia may not be associated with SK therapy since all patients received low-molecular weight heparin (LMWH) which is also known to cause thrombocytopenia[17] although to a much lesser extent than the standard unfractionated heparin.[18]

We also observed renal involvement in the form of subnephrotic proteinuria in two patients and non-oliguric ARF in a 47 year male patient. Proteinuria is common after SK treatment but it can uncommonly produce immune mediated glomerular injury leading to ARF, that is steroid responsive.[19] Our patient had spontaneous recovery of renal function and did not need any steroid or dialysis, therapy.

In AMI patients receiving thrombolysis, particularly elderly treated later than 12 hours, there has been excess of deaths in first 24 hours compared to controls, a phenomenon called "early hazard."[5] The exact mechanism of this early hazard is not clear, however various explanations include fatal ICH, myocardial rupture, reperfusion injury and inadequate reperfusion resulting in pump failure and cardiogenic shock.[20] Various studies[19] have reported equal incidence of side effects with intracoronary SK and intravenous anisoylated plasminogen streptokinase activator complex (APSAC) in AMI patients, with bleeding as the most frequently encountered adverse effect particularly from femoral puncture site for angiography.[21]

Unusual complications of thrombolytic therapy include aortic dissection, splenic rupture and cholesterol embolization. To reduce the incidence of side effects of SK certain modifications of the drug like, light B chain SK, activator-complex and acylated activator therapy have been proposed.20 None of these preparations are available in India at present.

The study has several limitations; firstly, there was no control group that makes any attempt to qualitatively or quantitatively assess adverse effects difficult. However, since the efficacy of SK has been established, a placebo group could not be included. Secondly, it would have been appropriate to compare SK with alteplase as regards efficacy, safety and cost. This could serve as a useful guide for practitioners of developing nations regarding the cost-effectiveness of the two agents since there is a 12-fold difference in their retail price (approximately US$ 50 per 1.5 million units of SK versus US $600 per 50 mg of rtPA). However, no company would be willing to sponsor such a trial, and there will be few patients who can actually afford alteplase in order to carry out an open study.

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COMPUTERIZED TOMOGRAPHY IN EVALUATION OF CHILDREN WITH PARTIAL SEIZURES

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ABSTRACT

Seizure disorder is common in children. Partial seizures are more frequent, and in the developing world, mostly have an underlying pathology which can be discerned if appropriate investigations are conducted. Majority of doctors depend on x-ray skull & EEG to dig out a cause but fail. Computed axial tomography (CAT) is not routinely included in the diagnostic workout. The paper aims to assess the need and benefits of a routine CT in a child presenting with seizures.

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INTRODUCTION

Seizure disorder, the clinical expression of a sudden, excessive, paroxysmal, discharge in the grey matter, is common in the developing world, particularly in children with an average incidence of 8%. Largely considered to be idiopathic (primary), an appreciable number, when properly investigated, reveal an underlying cause, ranging anywhere from infection to tumours (1). More than 40% of pediatric seizures are partial, which are more often associated with some underlying treatable pathology as tuberculomas, abscesses, tumours, arterio-venous malformations etc.(2). Management of patients with or without a discernible cause varies greatly as does the prognosis. Thus, identification of some discernible, treatable pathology in a patient with seizures is of paramount importance. Electrencephalography, a favourite of pediatricians & neurologists for identifying underlying causes, is nonspecific, with results being normal or equivocal in as many as 20% of such cases(3). Plain X-rays are even more unreliable, and may miss any lesion unaccompanied by calcifications (4).

Computerized axial transverse scanning, now increasingly used for finding out underlying causes of seizures, has greatly eased management of seizures, since about 30% of seizure disorders reveal structural abnormalities on CT scanning. The greater yield has prompted many experts to include CT in routine investigation of any seizure disorder especially the partial seizures(5). However, despite being much more economical than MRI, the CT is still unaffordable to the masses, and while the facilities are now being made available increasingly in urban areas, the vast populations of rural areas have no access to it. The present study was, therefore, conducted to assess the benefits of including CT as a routine investigation for seizure disorders in children in our place.

SUBJECTS & METHODS:

Seventy children, aged 1 month to 14 years, with partial seizures but no associated mental retardation, metabolic disorder or acute cerebral insult, admitted in the pediatric wards of Government Medical College Hospital, Jammu, during 1999 and 2000 were subjected to neurological examination, chest & skull radiography, tuberculin test, EEG and CT scanning during the inter-ictal period. Figure 1 shows the age & sex break-up of the subjects.

RESULTS:

Analysis of data revealed that out of the 70 studied subjects, 40 (57%) had complex partial & 25 (36%) simple partial seizures, while 5 (7%) were suffering from focal seizures with secondary generalization. (Fig 2). In the majority of

Key words: Partial seizures in children, CAT scan findings, Utility of CT in pediatric seizures

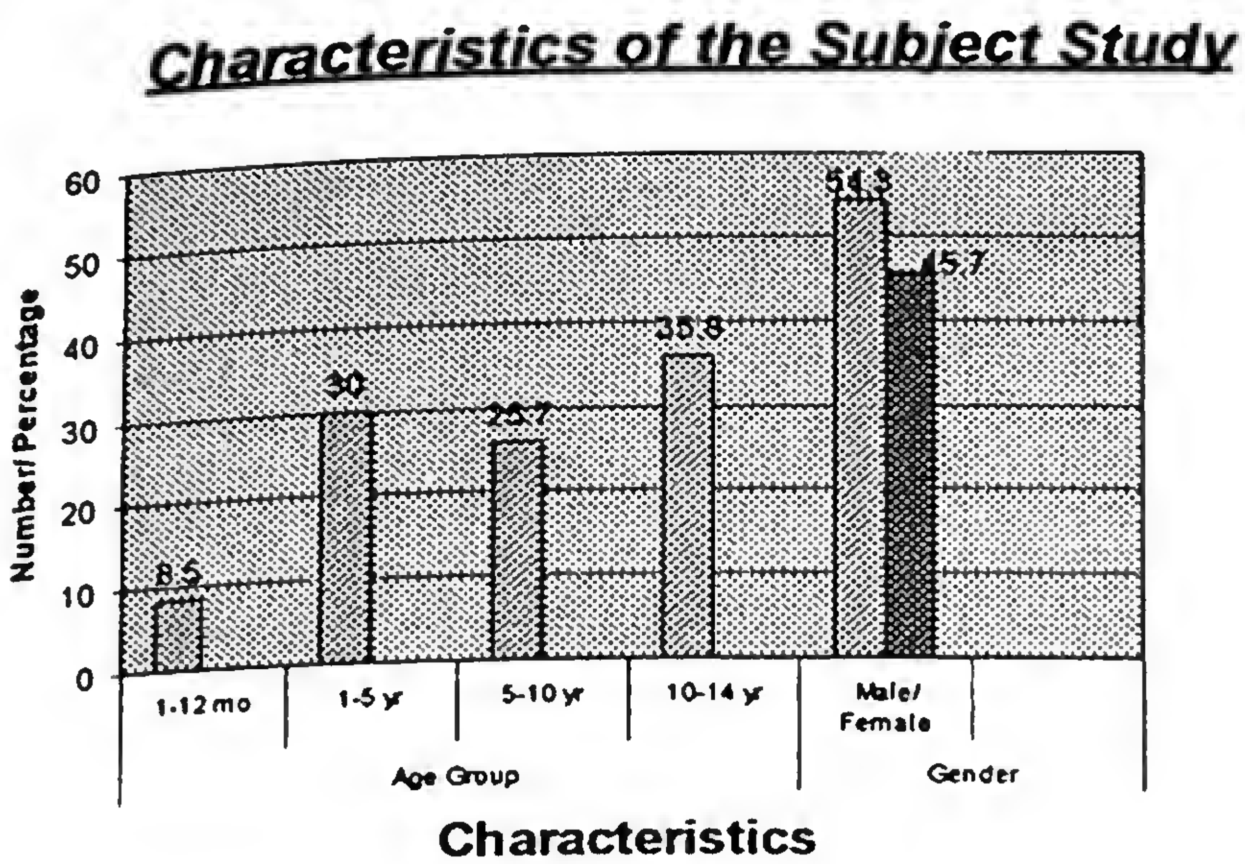

Fig. 1

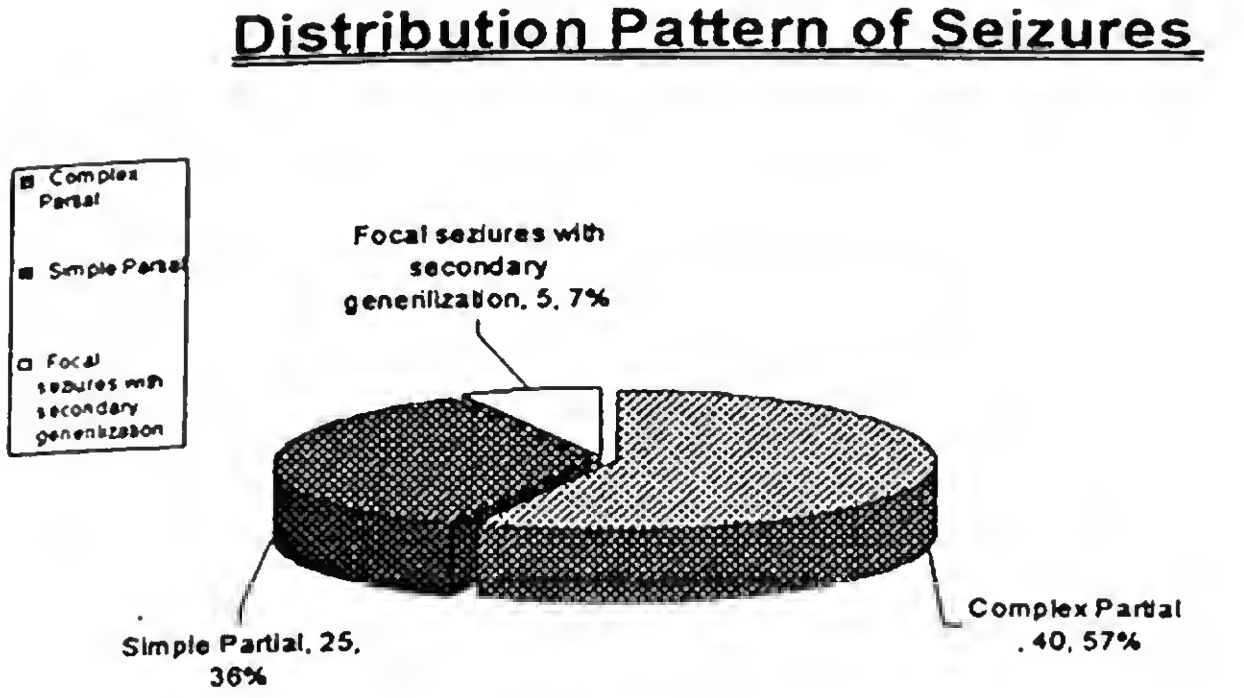

Fig. 2

cases (63.2%), no underlying risk factor could be found. However, in 10%-11% of cases, perinatal insult, family history of seizure disorder and previous occurrence of meningitis or encephalitis was reported. A previous history of febrile seizure or post-natal trauma were other less frequently cited (2.9% each) underlying risk factors. (Table 1). Neurological examination was abnormal only in 15.8% cases. Four patients (5.7%) showed a lesion on chest x-ray which included primary complex, non-resolving consolidation & pleural effusion. Plain x-ray of skull was abnormal only in 2 instances (one exhibiting fracture & another calcification). Tuberculin test was positive (10 mm or more) in 10% cases. Electroencephalogram, done 6 weeks after the seizure, was abnormal in 48 (68.5%) cases, mainly showing focal spike & wave discharge and focal slow waves. (Table 2)

Contrary to paucity of detectable abnormalities in other pertinent investigations, CT revealed some or the other abnormality in majority of cases (74.3%); only 25.7% were normal. The presence of a neurological abnormality on clinical examination or an abnormality in EEG greatly increased the chances of finding an abnormality on CT. More (80%) of patients with simple partial seizures showed an abnormality on CT than those with complex partial (72.5%) or focal with secondary generalization (60%). (Table III)

Table -1

Distribution Pattern of Seizures & Associated Risk Factors

Underlying Risk Factors	Percent of the Studied Subjects	
	No	(%)
• Perinatal insult	8	11
• Family history of epilepsy	7	10
• Previous CNS Infection Tuberculous Meningitis Pyogenic Meningitis or encephalitis	7	10
• Previous history of febrile convulsion	2	2.9
• Trauma	2	2.9
• Not known	44	63.2

Table -2

Interictal neurological examination, x-ray skull, x-ray chest & EEG

SN	Characteristic	Percent of the Studied Population	
		No	(%)
1.	Neurologic Examination		
	Normal	59	84.2
	Abnormal	11	15.8
2.	Chest Radiograph		
	Normal	66	94.3
	Abnormal	4	5.7
	Non resolving consolidation		
	Primary Complex		
	Pleural effusion		
3.	Skull x-ray		
	Normal	68	97.1
	Abnormal	2	2.9
	Calcification		
	Fracture		
4.	Tuberculin Test (Mantoux)		
	Negative	58	83
	Positive (10 mm or more)	12	17
5.	Interictal EEG		
	Normal	48	68.5
	Abnormal	22	31.5

The main lesion (found in 63.5% cases) was focal ring or disc enhancing lesion, followed, in order, by atrophy or a space-occupying lesion (9.6% each), calcification (5.6%), and intracranial hemorrhage, trauma or hydrocephalus (3.9% each). The commonest lesion, hypo-dense area on plain CT enhancing into small ring or disc-like lesions on contrast examination, were located mostly in parietal area, were sub-cortical & measured less than 10 mm in diameter. (Figure III).

DISCUSSION:

Partial epilepsy is common in childhood accounting globally for about 40%-45% of the pediatric seizure disorder. It is especially more frequent in developing countries, where it constitutes 2/3 of all seizures[6], because of a higher incidence of cortical insults from varied causes during prenatal, perinatal, and infancy periods[7]. In the pediatric age group, convulsions represent a confluence of age, heredity and structural abnormalities in brain, thus the modalities of diagnosis and management and prognosis are apt to be different and implications more serious than in adults[8]. Majority of partial seizures in children are secondary to treatable causes as tuberculomas, abscesses, tumours and arterio-venous malformations etc which makes detection of an underlying lesion even more vital. Till the early 1970s, approach to management of seizures in general, and of partial seizures in particular, was guided by the rare finding of an underlying abnormality on skull radiography or electro-encephalography. Since April 1972, Hounsfield & Cormack's breakthrough imaging technique, the computerized axial tomography, which can reconstruct the internal structure of an object from its multiple projections, has revolutionized the diagnosis and management of seizure disorder. Skull x-ray, traditionally used to locate a possible lesion, generally failed as it could not pick up lesions other than fracture and calcifications. They often failed even to detect smaller fractures. In our series, too, it failed to detect a fracture which was later made visible on CT. EEG is more sensitive in picking up an epileptic focus, but is non-specific and can not discern the nature of the lesion[3]. Also, diagnostic interictal EEG abnormalities are found more frequently in the generalized than in partial epilepsies[6]. Over the last 3 decades, the exposure time required for tomography has got reduced to a few seconds and at the same time, diagnostic precision has improved such that, in one study[9,10], 26% of lesions missed on such sensitive investigations as angiography were picked up by CT.

Table -3
CT Scan Findings & Its Relationship with Other Findings

SN	Relationships	Findings on CT Scan			
		Normal		Abnormal	
		No	(%)	No	(%)
1.	Overall	18	25.7	52	74.3
2.	Type of Seizures:				
	Complex Partial	11	27.5	29	72.5
	Simple Partial	5	20.0	20	80.0
	Focal with Secondary generalization	2	40.0	3	60.0
3.	Gender:				
	Males	10	26.3	28	73.7
	Females	8	25.0	24	75.0
4.	Age at Onset of Seizure:				
	1-12 mo	3	50.0	3	50.0
	1-5 yr	5	24.0	16	76.0
	5-10 yr	3	16.0	15	84.0
	10-14 yr	7	28.0	18	72.0
5.	Status of Interictal Neurological Examination:				
	Normal	17	28.8	42	71.2
	Abnormal	1	9.0	10	91.0
6.	Interictal EEG Findings:				
	Normal	11	50.0	11	50.0
	Abnormal	7	15.5	41	85.5

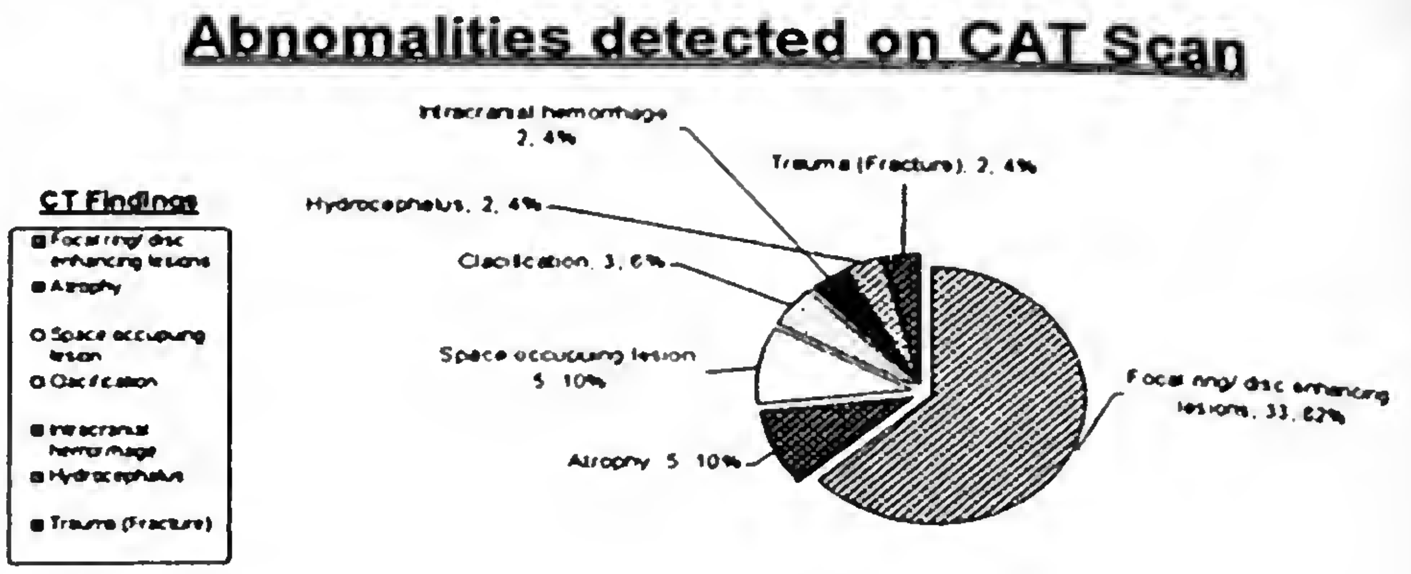

Fig. 3

Within 3 years after its introduction, CT began to be used extensively for unearthing structural lesions of brain. Bagdanoff & his colleagues (11) could unearth abnormalities in over 35% children with seizures; in focal lesions the yield was as high as 75%. Other researchers[12,13] had a similar experience. Houser and his colleagues who reviewed different contemporary reports in 1975 [14] to correlate CT findings with neuro-radiological, surgical and pathological findings, came to the conclusion that all corresponded significantly.

In almost 30%-35% of seizures in children, CT is able to pick up a structural abnormality, which may be treatable or untreatable. The yield has been seen to be much higher in partial (43%-63%) than in generalized (10%-32%) seizures. [15-20]. The yield in focal lesions has been as high as 71%-75% in different studies [11,18,19]. Studies which aimed at testing the value of routine CAT of brain in epilepsy [19-24] all came to the conclusion that CT was extremely useful in the diagnosis and management of partial seizures.

In our study children hospitalized for partial seizures without any associated neurological abnormality, mental retardation or biochemical disorder, 74.3% revealed some or the other abnormality on CT, which was much higher than the 22%-43% reported from the developed world [13,15,25], but compared well with 68%-73% detected in various Indian studies [26-30]. On further analysis, simple partial seizures showed a better yield (80%) as compared to 72% with complex partial seizures, being much higher than that reported for the either in Western studies[19,31,32].

Unlike the Western studies which mostly found atrophy (Diffuse or focal), porencephaly, hydrocephalus, or tumours as underlying lesions in partial seizures, Indian authors reported unique CT findings characterized by a focal ring or disc-enhancing lesion, usually less than 10 mm in diameter in size and cortical or sub-cortical in location. Curiously, these were the most frequent lesions detected in Indian studies, accounting for 24.8%-56% of lesions. [26,29,30,33]. Such lesions were mostly found to be inflammatory ie caused by tuberculomas, neurocysticercus granulomas, chronic pyogenic absecess, histoplasmosis, and blastomycosis. In our study, 63.5% of the abnormal scans (33 patients) were focal ring lesions, of which 18 turned out to be tubercular, 8 neuro-cysticercosis, 3 tumours, 2 abscesses, and one arterio-venous malformations.

Many recent studies have shown the benefits of CT over other customarily performed investigations in seizure patients[11-35], while others have strongly recommended routine use of CAT in every child with partial seizures[36]. In our series, too, CT scan was of direct therapeutic benefit to almost all patients with underlying abnormalities: the results justify its routine use in every case of seizure in pediatric age group. This is more pertinent in our place because MRI, though of higher diagnostic accuracy, is much more expensive, unaffordable & scarce than CT.

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CLINICAL PROFILE OF PERFORATING OCULAR INJURIES IN KASHMIR

Mufti Asmat, Nasti A.R., Ashai M., Qureshi T., Dar Saleema, Dar Ayub

ABSTRACT

Ocular injuries known from the early human life are increasingly becoming the cause of permanent blindness. Among the numerous underlying causes of the ocular injuries common causes of the perforating ocular injuries are related to the industrialization and the increasing violence of different kinds all over the world, and so in the Valley of Kashmir, where the Deptt. of Ophthalmology has entertained 46 Patients of severe perforating Ocular injuries out of a total of 41242 patients seen over a period of six months, and the very important and common cause was the blast injuries accounting for 21.73% of perforrating ocular injuries. Occupation related Ocular injuries were seen less commonly than accidental and non-occupational ocular injuries because of the absence of industrialization in the Valley. The patients who sought Medical advise soon after sustaining trauma had better out come than those who ignored the trauma for some time in the first instance.

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INTRODUCTION

Ocular injuries are known to the mankind right fromthe time of inception of human life itself. Ocular injuries are increasingly becoming the cause of permanent blindness. Perforating injuries in particular carry a high risk of visual morbidity in all age groups. (1) The frequency of eye injuries partiularly in first three decades of life is remarkably high and the damage caused is often so serious that it may produce a physical and psychological handicap for whole of the life. The pattern of the ocular injuries varies from area to area depending upon the activities of the people residing in a particular area.[2] Eye injuries are causing concern to the ophthalmologists allover the world, so is in the valley of Kashmir where the ocular injuries of serious nature have been showing a significant rise in frequency over the last more than a decade because of the present turmoil in the valley of Kashmir.

MATERIAL AND METHODS

Ophthalmology department of Govt. Medical College Srinagar is the apex Center of Ophthalmology in the valley of Kashmir. It is the only center which provides round the clock facilities for all kinds of ocular emergencies and it is responsible for all kinds of treatment ranging from conservative methods to the most modern and highly sophisticated surgical procedures. As such almost all cases of ocular injuries/emergencies are referred to this department from all over the valley.

Patients of the ocular injuries that were seen and admitted in the department of Ophthalmology from March 2001 to August 2001 were studied with the details of all necessary parameters including age, sex, residence, occupation, mode of injury, time of injury, place of injury, structures involved, hospital course and these patients were followed for six months after the discharge from the ward. Those patients who had very minor and trivial injuries and did not need admission in the hospital were not included in the study. Statistical data was analysed with reference to various parameters.

A detailed examination of the anterior segement of the eye and the ocular adnexa with special emphasis on the extent of the injury and damage to various ocular structures was done by general inspection in diffuse light and by slit lamp examination. A thorough examination of the conjunctiva, cornea, sclera, anterior

Key words: Perforation, ocular injuries, visual acuity.

Three patients had hospital stay of less than three days while as majority of the patients had hospital stay of more than 4 days which extended to more than a week in 20 patients.

On follow up complete vision or eye was lost in 9 patients (out of whom two were subjected to enucleation) twelve patients had visual acuity of less than 6/60, eight patients had visual acuity of 6/60-6/24 and ten patients had visual acuity of 6/18-6/9. Vision was unaffected in one patient who had a visual acuity of 6/6 and final vision could not be tested in six patients due to non-cooperation or some other reason.

DISCUSSION

The patients of severe ocular injuries comprised 0.21% of the total of 21421 outdoor and emergency room patients from March 2001 to August 2001. An incidence of 2.7% and 0.082% have been shown by Parmar et al (1985) and Malik respectively[1,2]. However, an earlier study conducted in Kashmir by Saleema et al (1987) has reported an incidence of 0.49% (including all types of Ocular injuries).[4] A very high incidence of 10% has been reported by Sorsby.[5] The incidence of perforating Ocular injuries varies from place to place according to the developmental status and activity pattern of the local population.[2] Majority of the patients 89.13% were below 40 years of age. It goes in conformity with other studies i.e., Malik et al who has reported 79.60% Ocular injuries in 1st three decades of life, also Parmer et al has reported 86.74% patients below 30 years of age.

Males were affected more frequently than females with a ratio of 4.75:1. The sex difference was seen in all age groups. The similar sex differences have been reported in other studies conducted in various parts of the country. Males are more commonly involved as they undertake more violent activities than females do.[6]

In occupational injuries (39.13%) those occuring in Masons and stone cutters (15.21%) were strikingly common (7 out of 18). Other occupations responsible were that of black smith and a commoner one related to agricultural activities. children had injuries related to sports activities. Youngest patient in this study was a 8 years old boy with penetrating eye injury caused while playing Gulli Danda. This statistical data about the aetiology of the penetrating eye injuries does not differ very significantly from what has been reported in other studies conducted earlier in Kashmir and other parts of the country with the exception of the present turmoil (in Kashmir Valley) related blast eye injuries accounting for as high as 21.73% of all patients involving both sexes and all age groups.

Industrial eye injuries are very rare in Kashmir due to the absence of industrialization while as in the industrialized areas such injuries have been reported to account for 12.24% to 15.40%.[7]

Cornea being the most exposed part of the globe was affected in 78.26% cases, lens and iris were next in fequency. Malik et al and Sarda et al have reported the Corneal involvement in 55.80% and 68.10% respectively while as Saleema et al has reported corneal involvement in 96.20% patients.

As reported in many other studies (i.e., Parmar et al, Saini et al, Malik et al) the present study has also revealed the involvement of the right eye as more common than the left eye[1,2,8]. In this study only 58.69% patients reported in 1st 24 hours, most of these patients had serious eye injuries either due to the firearm explosion or some oter cause, but it was observed that outcome was better in those patients who presented earlier as compared to the patients with similar injuries who presented late[9]. Complete loss of vision or eye was seen in the nine patients, seven of them had blast injuries, and other two patients with the perforating ocular injury of different cause also developed endophthalmitis and progressed to complete loss of vision.

SUMMARY

Among 46 patients with perforating eye injuries as many as 82.60% were males and majority belonged to the age group of less than 40 years. Occupational hazards related to agriculture and masonary were the main cause and among the accidental causes the firearm blasts were reponsible for a significant proportion of cases. Cornea, lens and iris were the most commonly affected structures. The patients presenting earlier had better outcome than those presenting late. Nine patients either lost the complete vision or the eye. Proper eye health education to the masses and awareness about the risk of eye injuries can prevent and minimize incidence of ocular injuries.

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SMALL GUT WORM OBSTRUCTION IN YOUNG ADULTS: AN EXPERIENCE AT SKIMS

Bhat Nadeem Ahmad, Nazir A. Wani, Tasaduq Ahmad, Samia Raheem, Zahid Zaide

ABSTRACT

Between March 2002 to March 2003, in 14 young adults who reported to SKIMS Accident and Emergency department with complaints suggestive of small gut obstruction. The small gut obstruction was proved to be due to round worm infestation. The present study analyses the management of these patients and underlines the need to recognise ascariasis as important cause of small gut obstruction adults.

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INTRODUCTION

One of the most common parastic infection in humans is ascariasis. In the uderdeveloped and developing world especially, ascariasis is a major cause of morbidity and mortality.

Infection occurs at all ages but is most common in children of preschool or early school age. Both sexes are equally affected[1]. Though more common in children, intestinal obstruction due to Ascaris lumbricoides in adults especially in young adults is also well known.

The present study is based on a series of 14 young adults who were managed as cases of intestinal obstruction due to Ascaris lumbricoides. Two patients were subject to surgery when enterotomy was done in one patient and ileal resection and anastomosis in another.

MATERIAL AND METHODS

The study is based on a series of 14 patients who reported to department of Accident and Emergency SKIMS between March 2002 to March 2003 with complaints suggestive of intestinal obstruction and were managed jointly by department of General Surgery and Department of Accident and Emergency. Majority of the patients presented as cases of subacute intestinal obstruction and were managed conservatively. Two patients needed laparotomy when enterotomy was done and obstructing boluses of worms removed in one patient and ileal resection with anastomosis was done in another. The average age of patients was 21 years. The most common presenting complaints were abdominal pain of colicky nature, nausea and vomiting, constipation. The average duration of complains was 5 days (range 2-17) days. The baseline investigations were normal except for reduced Hb levels in 9 patients. The biochemical investigations were also within normal limits. Other investigations performed were plain x-ray abdomen, USG abdomen.

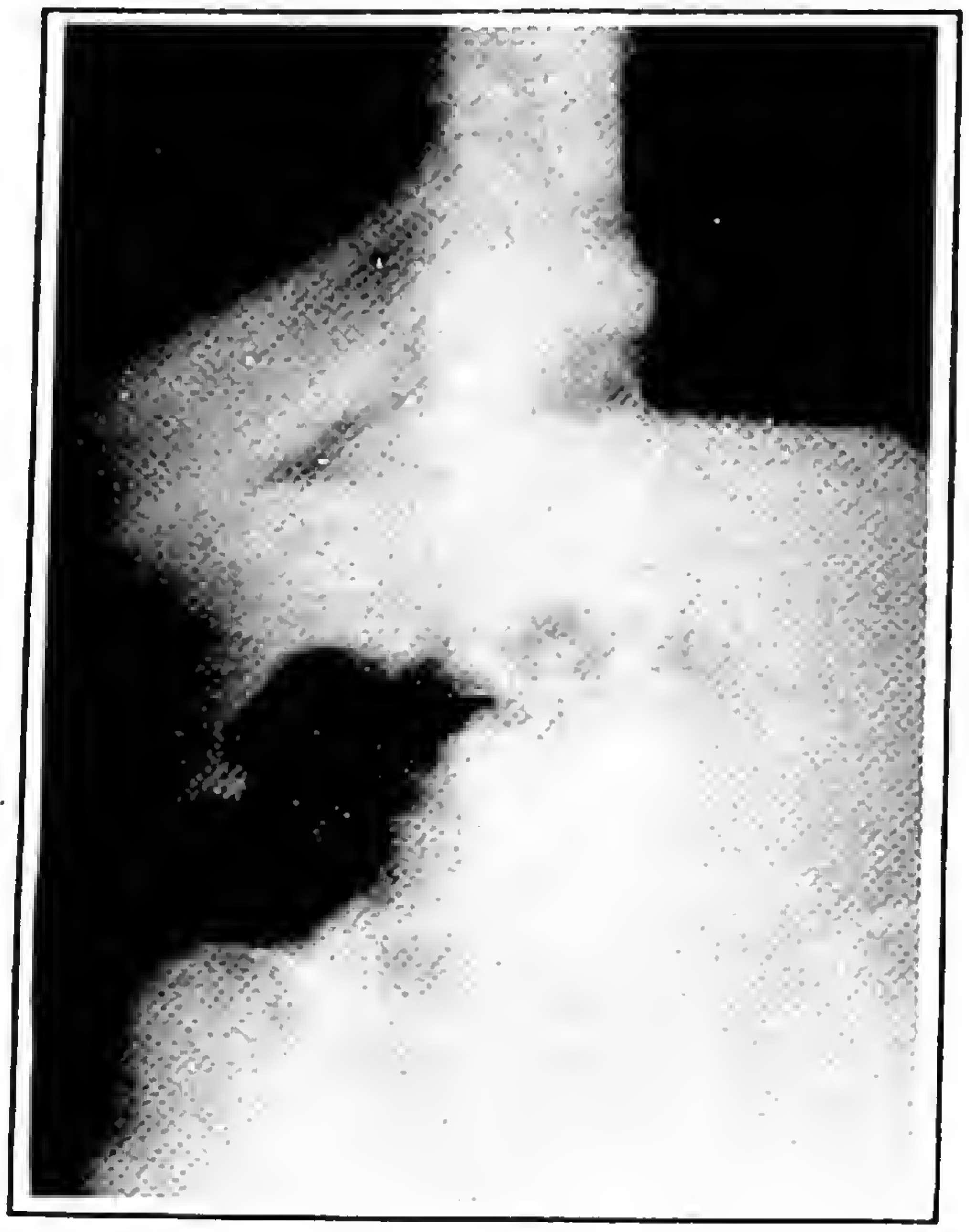
In a majority (9 patients) the x-ray abdomen showed obstructing worm boluses and the characteristics appearance of ground glass (Fig. 1)

The standard management for small gut obstruction was instituted, this included nasogastric aspiration, IV fluids and broad spectrum IV antibiotics. Proctoclysis enemas were administered in 10 patients twice a day.

Most of the patients showed improvement in symptoms and signs on the second day and five patients deflated. The treatment needed to be continued for another 2 days for the rest of the patients and by 5th day of admission there was significant improvement in the clinical picture and out of 14 patients 9 passed worms with stools. Two patients did not deflate and developed signs of abdominal tenderness and rigidity. These 2 patients were prepared for surgery. Adequate fluids and electrolytes were administered before surgery.

Key words: Ascaris, intestinal obstruction, enema, enterotomy

Lapartomy revealed small intestinal loops filled with worm masses. Some areas especially nearer the ileocaeccal valve were completely packed with worm boluses.



Attempts at manipulation and advancement in to the large gut were not successful. In one patient a transverse enterotomy was performed at two places, worm masses were removed. Care was taken to prevent any contamination of the peritoneal cavity due to spillage. The enterotomy was closed back in two layers. The second case needed a resection of small length of ileum, because of gangrenous changes, removal of worm masses, end to end ileo-ileal anastomosis and layered closure of abdominal wound over a CRD. The CRD was removed on third post operative day. This patient stayed febrile till 5th postoperative day. Intravenous antibiotics covering gram negative as well as anaerobes were administered upto 8th postoperative day. However, patients clinical condition continued improving with every passing day. Patient tolerated liquid diet by 10th postoperative day.

CONCLUSION

One fourth of the world population is infested with Ascaris limbricoides. There are approximately 4 million cases in United States[2]. The infection is usually transmitted via ingestion of eggs from contaminated food stuffs, infection may occasionally occur via inhalation of eggs and swallowing of infected secretions[3].

Infestation with ascaris is largely asymptomaytic, most of the patients have mild to moderate symptoms only, colicky abdominal pain being the most common complaint. The most common mode of management is conservative and about 80% of the patients are managed conservatiely with nasogastric suction and intravenous infusion[4]. However, all patients who present in the Accident and Emergency department, need to be observed closely while under conservative management for any signs of developing intestinal obstruction and complications like volvulus gangrene gut, perforation and peritonitis. Careful and timely decisions for surgery need to be taken in cases of intestinal obstruction so that pressure necrosis of intestinal wall, volvulus with resultant gangrene and toxaemia as a systemic complication may be prevented.

The symptoms and signs due to worm obstruction are classically colicky abdominal pain, vomiting and constipation. Patient may vomit worms. The worm masses may or may not be palpable. Digital rectal examination does not reveal much, worm masses may be palpated on DRE. The total white cell count may be raised, x-ray abdomen shows worms masses with characteristic appearance and in case of significat small gut obstruction, multiple air fluid levels may be seen.

As stressed before conservative management is the preferred course but close observation is needed so that surgery is done when needed. Antihelminthic drugs are better avoided in patients with severe abdominal pain or signs of subacute intestinal obstruction. Until pain has subsided and worm masses have disappeared or reduced in size on nasogastric aspiration, IV fluids and electrolyte replacement.

Management of small gut obstruction due to ascaris is an important surgical task. Though the incidence of worms causing small gut obstruction in young adults is small compared to children, but even in adults important decisions need to be made at appropriate time regarding surgery and the optimal surgical procedure needed to prevent complication that can result in significant morbidity and mortality.

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ANEURYSM OF THE SINUS OF VALSALVA EXTENDING INTO INTERVENTRICULAR SEPTUM: A RARE CAUSE OF COMPLETE HEART BLOCK AND ACUTE MYOCARDIAL INFARCTION

Nisar. A. Tramboo, Khurshid Iqbal, Bashir A. Naikoo, Khalid Mohi-ud-din, Mehbood A. Dar, Aejaz Ahmad Lone, Syed Monzoor Ali

ABSTRACT

Dissection of interventricular septum by aneurysm of the sinus of valsalva is extremely rare[1]. Extension into interventricular septum can lead to complete heart block by compression of the AV nodal/His bundle system[2]. We report a pateint with complete heart block and acute anteroseptal myocardial infarction caused by extension of a congenital sinus of valsalva aneurysm into the upper interventricular septum in a young male.

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INTRODUCTION

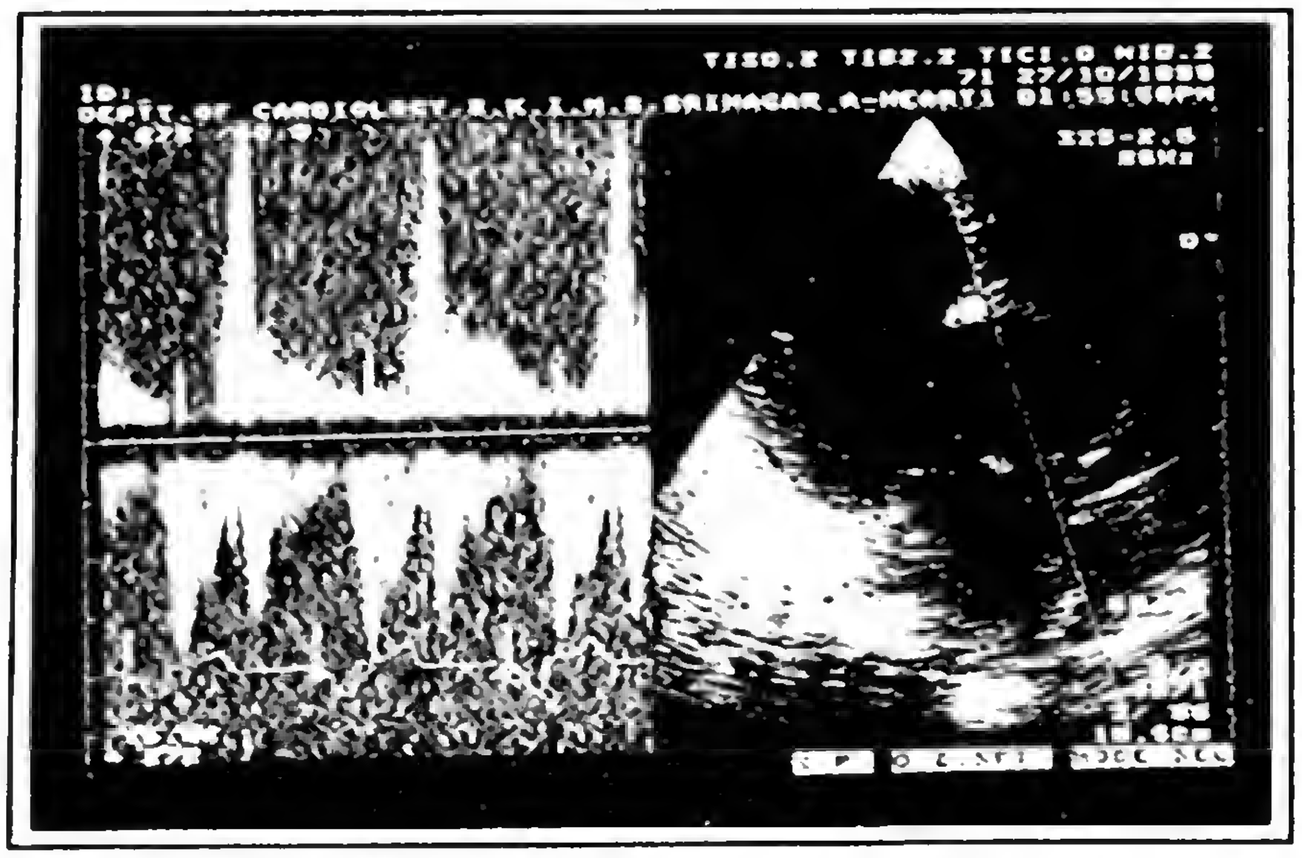
Aneurysm of the sinus of valsalva is an uncommon anomaly that occurs three times more often in males than in femals. The aneurysmal dilatation is progressive and may be clinically and hemodynamically silent. It is the rupture of sinus of valsalva aneurysm which produces significant hemodynamic abnormalities. It is very rare that the unruptured aneurysm may produce pressure symptoms in the form of conduction abnormalities and myocardial ischemia due to coronary arterial compression[3]. This report describes a patient who had interventricular septal expansion of the sinus valsalva aneurysm leading to complete heart block and anteroseptal myocardial infarction. We also emphasize the rarity of this condition and the value of transesophageal echocardiography in providing a complete anatomicofunctional characterization.

CASE REPORT

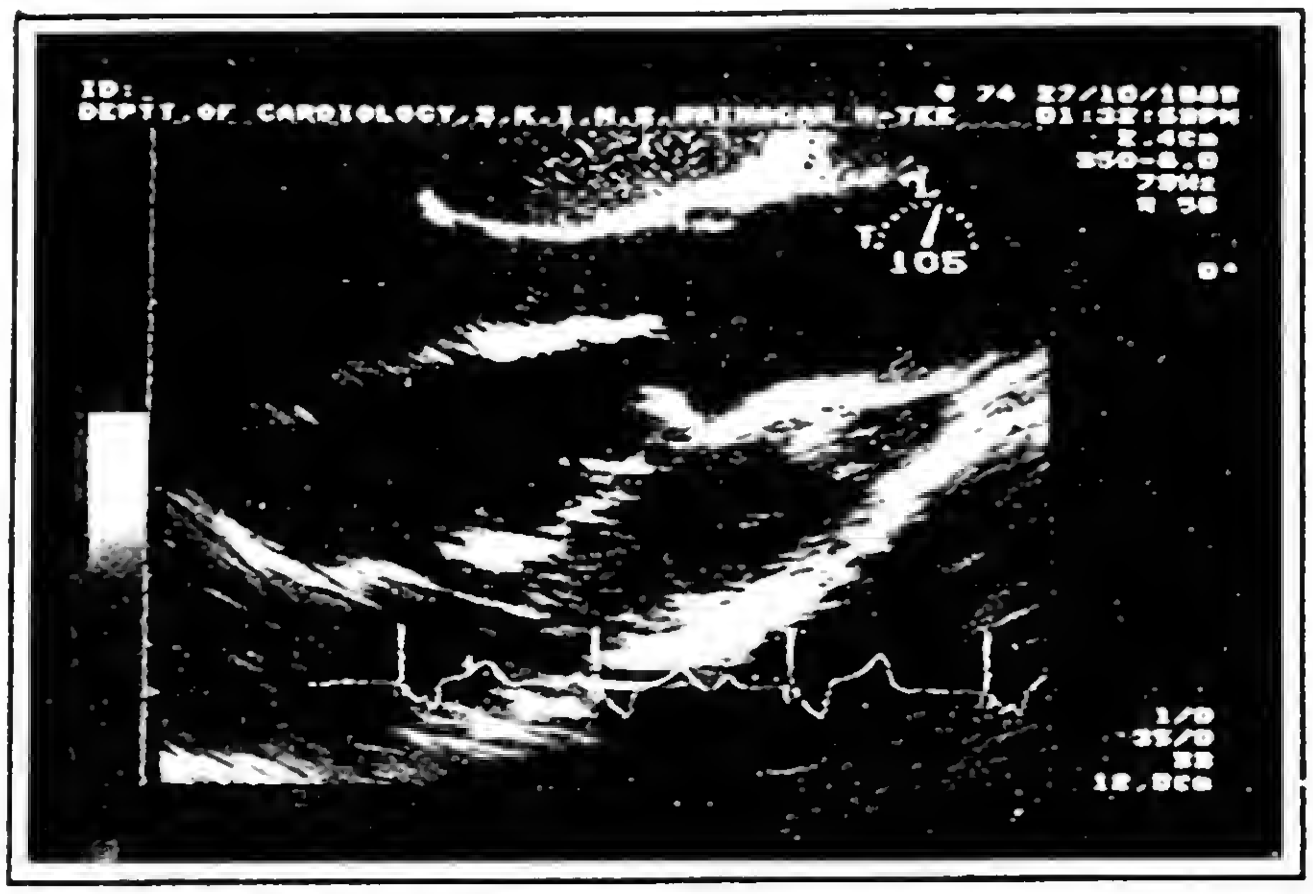
A 30 years old male reported to the Cardiology unit of Sher-i-Kashmir Institute of Medical Sciences, Srinagar with complaints of acute retrosternal chest pain and syncopal attacks. His examination revealed a lean built young male. His pulse was 40 beats per minute and blooc pressure 130/70 mmHg. His jugular venous pressure revealed intermittent cannon waves. Cardiac examination revealed a left ventricular third heart sound and grade II/VI systolic murmur of ejection quality, along the left sternal edge. There was no pericardial rub. Investigations revealed normal hemogram and urine examination. Fasting blood glucose and lipids were within normal limits. Serum CPK levels were 1015 IU(n=23-195 IU/L), Serum LDH was 850 IU/L (n=50-450 IU/L), SGOT was 150 U/L (n=0-40 IU/L). His ECG revealed complete heart block with a ventricular rate of 40/mt. Anterior procordial leads revealed marked ST segment elevation. His Doppler examination was performed on Toshiba Power Vision colour Doppler system. Transthoracic echocardiography revealed akinesia of interventricular septum and adjoining left ventricular free wall, left ventricular ejection fraction as calculated by modified Simpson's formula ws 42%. A large sinus of "valsalva" aneurysm (2.5 x 2 cm x 1.5 cm) was seen which eroded into upper interventricular septum. Doppler interrogation did not reveal any evidence of rupture of the aneurysm and showed systolic forward and diastolic backward flow (figure 1) suggesting that the blood was entering and existing the aneurysmal sac into aorta during diastole and systole respectively. Selected multiplane TEE views revealed aneurysm of right coronary sinus valsalva extending into upper interventricular septum (figure 2) and Doppler interrogation did not reveal any VSD or rupture of aneurysm into any cardiac chamber. In addition, color flow imaging

Key words: Aneurysm of Sinus of Valsalva, Complete heart block, Acute myocardial infarction.

revealed mild aortic regurgitation.



1. Transesophageal echocardiograph showing systolic forward and diastolic backward flow.



2. Transesophageal echocardiograph showing aneurysm of right coronary sinus of valsalva extending into upper interventricular septum.

DISCUSSION

Aneurysm of sinus valsalva is an uncommon disorder mostly arising due to congenital defect in the continuity between aortic media and aortic valve annulus[4]. The unruptured aneurysms are usually asymptomatic and diagnosed serendipitously. however, such aneurysms may produce cardiac ischemia. Rupture of sinus of valsalva aneurysm usually presents with sudden onset chest pain which soon gives way to right heart failure[2], since the right sided chambers are the most common receiving compartments. In our patient the unruptured right sided coronary sinus aneurysm dissected into upper interventricular septum and had led to complete heart block by compressing the AV node/ His bundle conduction system[2]. Such an occurrence has been reported previously[5]. Cardiac ischemia due to sinus of valsalva aneurysm may be caused by direct compression or distortion of coronary artery and diastolic filling of the aneurysm may provoke steal phenomenon resulting in reduced coronary artery perfusion[4]. Intermittent coronary osteal obstruction produced by the aneurysmal membrane prolapsing into aortic valve may produce myocardial ischemia and possible infarction[4]. In our case the acute anteroseptal myocardial infarction seems to have resulted from direct compression of the LAD branch of the left coronary artery since no freely moving flap could be visualized. Furthermore, the combination of acute anteroseptal myocardial infarction and complete heart block in a single patient with aneurysm of sinus of valsalva was not reported previously to the best of our knowledge. The patient was implanted a VVI MP bipolar pacemaker. He was advised corrective surgery, but the patient refused the same for personal reasons. Further the excellent anatomical and functional characterization in this disorder by the transesophageal echocardiography testifies the great diagnostic potential.

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AN UNUSUAL ABDOMINAL LUMP

Masood Iqbal, M. Ashraf Lone, M.N. Ahmad

ABSTRACT

A 55 year old male presented with distension of central abdomen of 5 day duration alongwith dull pain in abdomen and high grade fever of same duration. USG of abdomen showed a large cystic lesion in abdomino-pelvic position measuring 14.8 x 16.75 cm anterior to great vessels with low-level echoes. ELISA for hydatid serology was negative. CT scan of abdomen showed a huge cystic mass in mid abdomen mostly around umbilical area having attenuation of (+27 haemorrhagic) with septae measuring 17.7 x 8.9 cm. Intra operatively a large cystic mass was seen arising fromthe greater curvature of stomach embedded between the layers of greater omentum containing haemorrhagic fluid. Surgical resection of the mass alongwith the part of greater curvature of stomach was performed. Biopsy of the specimen suggested gastrointestinal stromal tumour with focal smooth differentiation, leiomyosarcoma can be considered. Patient is doing well more than a year after surgery.

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A 55 year old male presented with self-detected distension of central abdomen, dull pain in same area, high-grade fever of 5 -day duration. No history of any weight loss, malaise or any feature of upper GI bleed.

EXAMINATION:

Patient appeared well built with slight pallor, no cyanosis, jaundice or any lymphadenopathy. Patient was febrile with temperature of 101 F, pulse 100/minute, BP 110/70 mm of Hg. Abdominal examination revealed a huge intra-abdominal lump occupying epigastric, umbilical, and left hypochondrial regions. The mass was non-pulsatile, soft, smooth, non-tender, and mobile in transverse direction. There was no sign of ascites. Rest of the abdomen and other organs showed no apparent clinical abnormality.

INVESTIGATIONS

Routine haemogram showed anaemia (Hb - 6.8g/dl). Other routine biochemical examination of blood and skiagram of chest were normal. USG of the abdomen revealed a large cystic mass in central abdomen measuring 14.8 x 16.75 cm (Fig. I) anterior to the great vessels with low-level echoes and infolding of membranes (Fig. II). No ascites or liver metastasis was detected. CT scan after administering oral and intravenous contrast showed a well-defined cystic mass measuring 17.7 x 8.9 cm peri-umblical region having an attenuation of +27 (haemorrhagic). (Fig.III) Gut loops were pushed laterally. Rest of viscera appeared normal.

SURGERY:

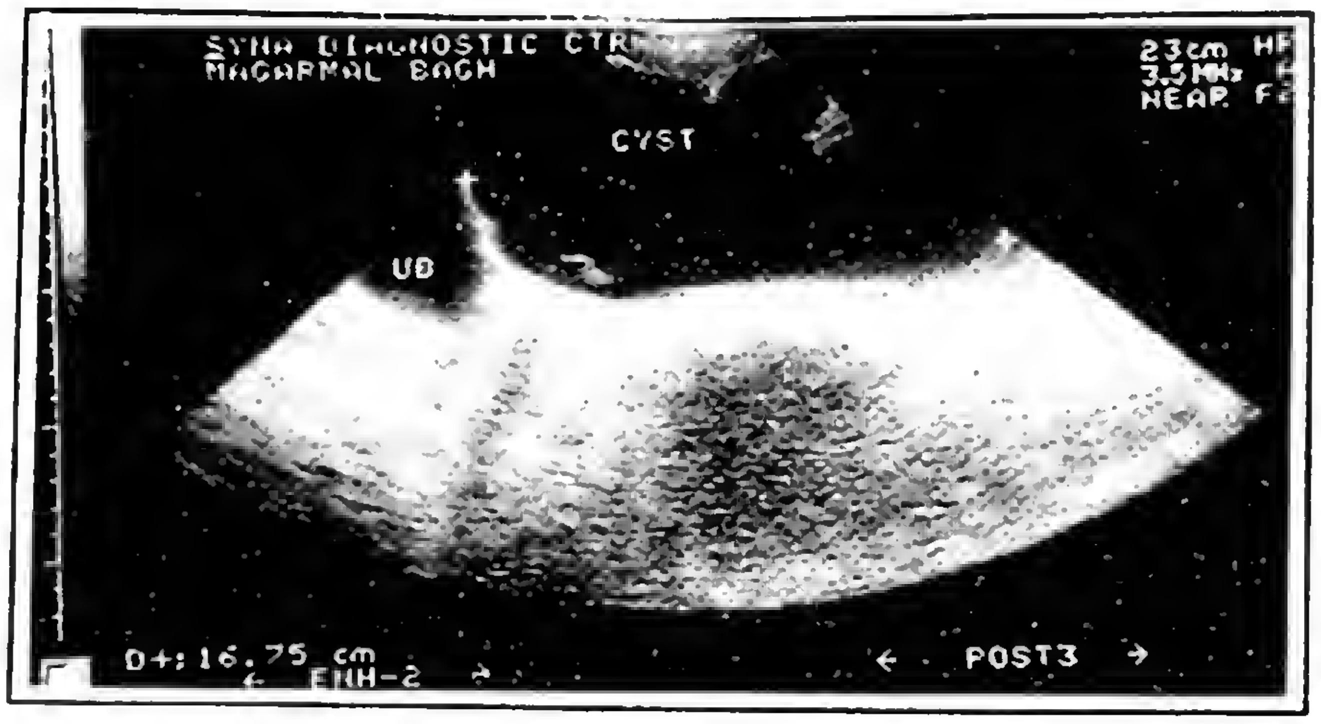
Exploration of abdomen was done after correction of anaemia through a right paramedian incision. A large haemorrhagic cyst was found arising from the greater curve of stomach encysted in the leaves of greater omentum. Cyst wall was soft, nodular and fleshy. It was not adherent to any neighbouring viscera. Excision of mass alongwith the part of greater curvature of stomach were it was attached to it was done. Postoperative recovery of patient was uneventful. Stitches were removed on 10th POD and discharged from the hospital.

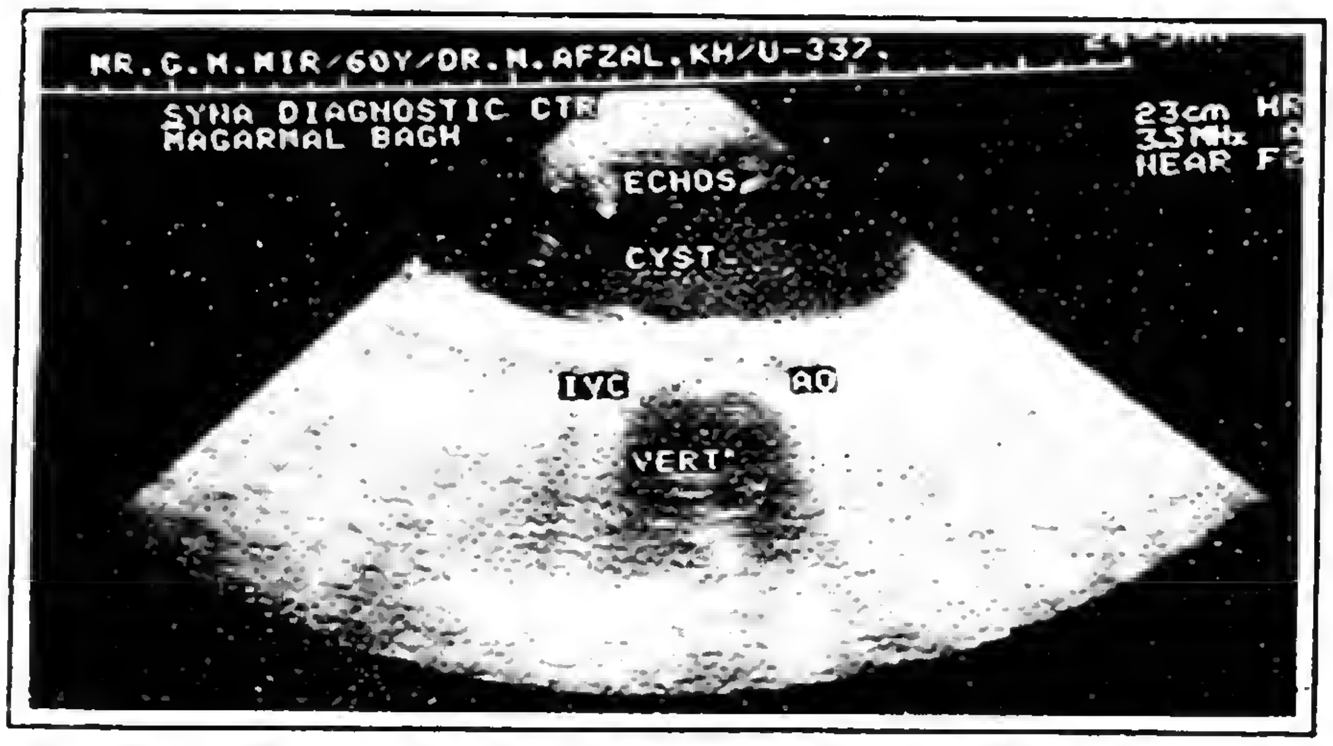
PATHOLOGY:

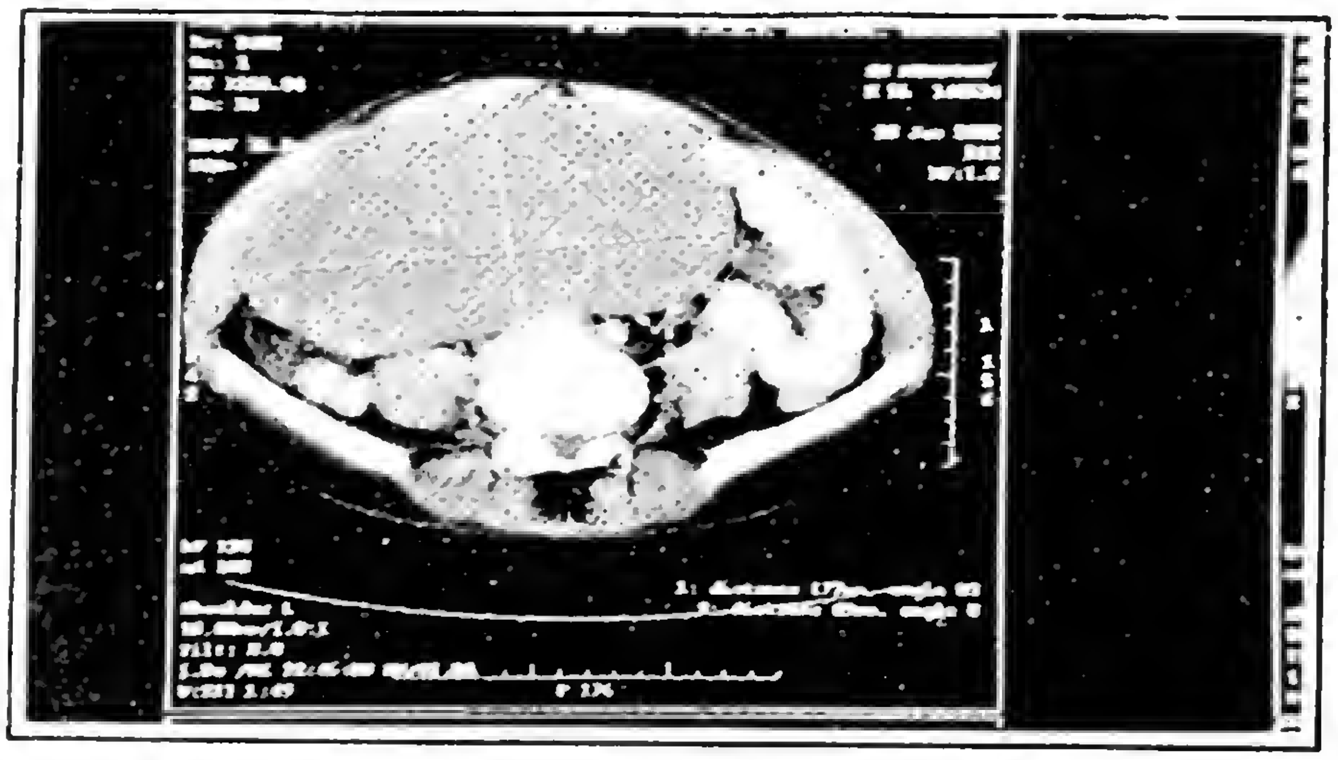
The surface of the tumour was nodular. Cut section was greyish white and stained with blood. Microscopic examination of various sections from

Key words: Gastro-intestinal stromal tumour, leiomyosarcoma, stomach, maligant.

different sites of tumour revealed features of leiomyosarcoma with areas of haemorrhage and myxoid degeneration. Mitotic rate was 5-7/10 HPF in mitotically active areas. Immunohistochemically the cells were found focally positive for smooth muscle Actin.







FOLLOW UP:

During the last check up which occured more than 8 months after the surgery the patient was doing well without any evidence of recurrence of the tumour.

DISCUSSION:

Gastrointestinal stromal tumours are uncommon mesenchimal tumours that arise in the wall of the gastrointestinal tract. They account for approximtely 0.1% to 3% of all gastrointestinal neoplasms, with about 150 new cases per year diagnosed in the United States. The term GIST first used by Mazur and Clark in 1983 includes a heterogeneous group of nonepithelial neoplasms with spindle or epitheliod cells, which display a range of differentiation[1]. It is difficult to determine microscipically the exact origin of these tumours. They have a complicated histogenesis and moreover it is not easy to assign a benign or malignant classification; for these reasons the non-specific term Gastrointestinal stromal tumour, GIST has been coined[2] Immunohistochemistry and features (smooth muscle GISTs), neural attributes (gastrointestinal anatomic nerve tumour), or characteristic of both muscle and nerver (mixed GISTs), or may lack differentiation (GISTs not otherwise specified). The Cajal cell, an intestinal pacemaker cell, has been proposed the cellular origin of GISTs, having both cell makers in common[3]. No histoloigic grading system has been established for this group of tumours[4]. Grossly GISTs are smooth grey-white tumours which arise within the muscularis propria of the GI tract. They are well circumscribed and contain a pseudocapsule. They may grow in an endophytic fashion compromising bowel lumen patency or may exhibit an exophytic or dumbell growth pattern. In GISTs with an endophytic component, the submucosal mass may have an overlying mucosal necrosis and ulceration. At a intraoperative appearance it is possible to distinguish a mass attached to the stomach or the bowel wall projecting into the abdominal cavity, displacing other organs as was seen in our case.[2] The mean age of patients is 58.5 years (range 22-79 years).[5] The risk factors and aetiology of GISTs remain undetermined[2]. Because of the non-specific symptoms, a delayed diagnosis is generally associated with Gastrointestinal stromal tumours, with a mean duration of symptoms before presentation of 6 months. The most frequent clinical manifestations are gastrointestinal bleeding, a palpable mass and mild abdominal pain in order of frequency[5]. The most frequent diagnostic test is CT; it can demonstrate a mass lesion, the contagious organ invasion and distant metastases. CT (in particular spiral CT scan with thin cuts) is the most sensitive test for the detection and gastrointestinal contrast study, abdominal ultrasound scanning, angiography).[5] The most common anatomic locations are the stomach (53%), the small intestine (33%), rectum (5%), oesophagus (5%) and colon (4%). The location of the tumour is not considered a significant prognostic factor[5]. Until more effective adjuvant therapy becomes available, the treatment of GISTs remains primarily surgical. Every effort necessitating the removal of adjacent organs. Incomplete resection should be performed only for the palliation of symptoms due to bleeding, pain, or mass effect[3]. It is essential to avoid tumour spillage or tumour rupture in the abdomen. They have been associated with an increased risk of peritoneal recurrence[2]. Systematic lymph node dissection is not thought to be neceesary.[6] The overall survival rate for all patients has been 35% at 5 years. Patients with complete resection had a 54% 5 year survival rate. Patients who could not undergo complete resection had a median survival of only 12 months; median survival was 19 months in those with metastases and 12 months in those with local recurrence. In the patients without metastases and who underwent complete gross resection size has been an important predictor of survival on both univariate and multivariate analysis. Tumour size >10cm has been the most significant factor. The status of the microscopic margin of resection does not affect survival. Many of this tumours are exophytic and protrude into the abdominal cavity, therefore, the microscopic margin of resection may not be as important as whether the tumour sheds cells directly into the peritoneal cavity[3]. The follow up of patients with curatively resected primary gastrointestinal sarcoma is a combination of clinical and appropriate imaging directed to the early identification of a small group of patients in whom failure is confined to the liver and in whom the potential for liver resection exists[4]. There is currently no strong data to support the use of chemotherapy, other than in a controlled trial.

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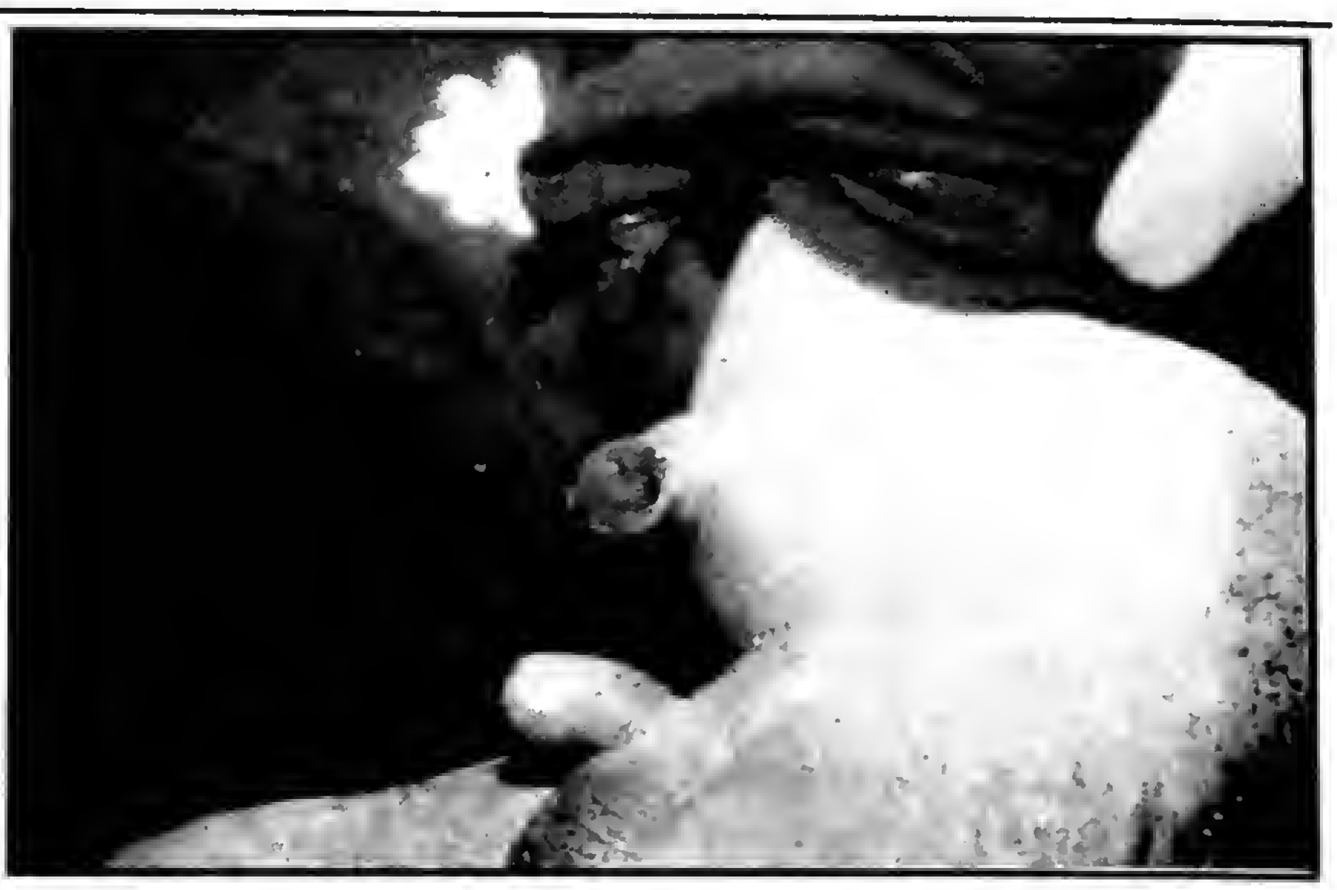
PATENT VITELLINE DUCT WITH CUTANEOUS FISTULA

Ishtyak Ahmad Mir MB, CDM, FAIC, FICS



Patent vitellointestinal duct with cutaneous fistala excoriation of the skin is seen.

Patent vitellointestinal duct after anastomosis

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3 days old child was brought by his parents with complaints of passing fecal matter through umbilicus since birth. He was also passing fecal matter per rectum. The abdominal wall used to be drenched with intestinal contents. On examination child was ill looking, infraumbilical part of abdomen was stained with intestinal contents and there was excoriation of the abdominal skin. Haemogram, X-Ray Chest and abdomen and blood grouping was done. All measures to manage the patient conservatively failed and he was operated at the age of 17 days. Operative findings were patent vitello-intestinal duct (Fig. 1), with cutaneous fistula. The whole circumference of fistula was communicating with the skin. The base of the defect was about 1 cms. The edges were fashioned and after thorough wash, end to end anastomosis was done (Fig. 2). The child was discharged on 5th postoperative day. The child is doing well at a follow up of 4 years now. There are many possible abnormalities which have been classified, typical variations of the pathologic varieties are well known and established facts.[1-2]

If the vitelline duct is patent from the terminal ileum to the umbilicus, fecal umbilical drainage will be noted. The diagnosis of such a problem is made easily and surgical correction is curative. However management at a good centre by a specialized professional is mandatory.

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INTESTINAL METAPLASIA AND GASTRIC CARCINOMAS

Cancer of the stomach is one of the commonest and most serious forms of malignant disease in native population of Kashmir, India. Durrani et al[1] have reported cancer of the stomach as the most frequent neoplasm of gastro intestinal tract in Kashmir.

Atropic gastritis with intestinal metaplasia (H&E-100X)

Khuroo et al[2] reported an incidence of esophageal and gastric carcinomas as 27 per hundred thousand in a population based study. Such an incidence is comparable to high prevelance areas of the world such as China, Japan, and Iceland.

In a study 100 cases selected over a period of one year, patients were subjected to endoscopy, (79 males and 21 females) and were subsequently confirmed as cases of gastric carcinoma under light microscopy.

Endoscopic biopsies were taken from the growth as well as from the mucosa immediately surrounding the lesion and at a distance of 1 cm from the growth. Routine paraffin blocks were made after the tissues were fixed in 10% neutral formalin and processed in automatic tissue processor. Three to four micron thick sections were cut and stained by Haematoxylin and Eosin stain. Special stains were employed wherever necessary.

Gastric carcinomas were classified as per the classification of Lauren M[3,4] into Intestinal type of gastric carcinoma (IGC) and Diffuse type of gastric carcinoma (DGC). Mucosal changes such as intestinal metaplasia, wherever present, was graded as per Schindler quoted by Sipponen et al[5].

Of these 100 cases of gastric carcinomas visualized on endoscopic examination, 78 tomors were in the distal portion of the stomach and 22 were in the proximal. The adjacent mucosal changes were studied and intestinal metaplasia was observed in 68 cases on light microscopy. The extent of metaplasia was grade IV and was associated with intestinal type of gastric carcinoma.

The incidence of intestinal metaplasia in this study was more common in men (52 percent) in comparison to females (16 percent) and the age group mostly involved was 51-60 years.

Chronic gastritis, which includes atrophic type and intestinal metaplasia are considered to be etiopathogenetically related to gastric carcinomas. The main reason for such assumption has been the prevelence of intestinal metaplasia present in the adjacent mucosa surrounding the tumor, through intestinal metaplasia is age related as observed in this study and the change was predominant in the intestinal type of gastric carcinoma.

We observed a high prevelence of intestinal metaplasia in gastric carcinomas. The correlation of intestinal metaplasia depended upon the location and type of gastric carcinoma. Of the 78 cases of gastric carcinoma in the distal portion of the stomach 42 were IGC type and 36 of DGC type. The intestinal metaplastic changes were predominant in IGC type of gastric carcinoma of distal location.

It was further observed that the intestinal metaplasia in the mucosa adjacent to the tumor or 1 cm away from it was quite significant and was more pronounced in the antral mucosa surrounding the tumur. Thus intestinal metaplastic changes provide the evidence of the existence of some casual relationship with gastric carcinomas because of the fact that 68% of the cases in this study showed metaplastic changes in the mucosa surrounding the tumor.

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ANTHRAX REVISITED

Anthrax although primarily an animal disease, is still common in developing and underdeveloped nations. It is potentially a fatal disease and may result in life-threatening complications if the intervention therapy is delayed. A case of a 15 year old boy from rural area of Kashmir, India is reported here.

The boy presented with a 4 day history of swelling of the right side of face. He developed a painless nodule above the right eyebrow which gradually enlarged and ulcerated with surrounding edema and erythema. He had no fever, vomiting, cough or diarrhea. Examination showed multiple vesicles with serous fluid on the face. There was no pain on scrapping the lesion. There was no lymphadenopathy or lymphangitis. Chest radiographs were unremarkable. He has no other significant medical or surgical history. He was treated with intravenous crystalline pencillin and Gentamycin and is currently doing well. He did not have any exposure to animals or animal products. However, patient did not give any history of injury at the site of lesion. Patient used to visit his orchards off and on. Microbiology examination of a direct smear with a Gram's stain showed Gram-positive rods with characteristic squared ends arranged singly, in pairs and in short chains. No pus cells were seen. Giemsa stain showed highly refractile capsule. No eosinophils were detected.

Anthrax still remains a common disease in animals and humans in the underdeveloped and developing countries. The disease has been described as far back as the ancient period. The term "anthrax," is derived from the Greek anthrakites ("coal-like"), referring to the typical black eschar seen in cutaneous involvement. In the 9th century, it served as the prototype for Koch's postulates regarding the causation of infectious disease. The first vaccine containing attenuated live organisms was Louis Pasteur's veterinary anthrax vaccin[1]. It is a highly virulent and contagious disease caused by the Gram positive toxigenic spore-forming Bacillus anthracis. It is a large (5-8μm x 1-1.2μm), non-motile, aerobic, rod-shaped, bacterium. It forms spores, which can survive for years in the environment. Capsular polypeptide and anthrax toxin are the principal virulence factors of Bacillus anthracis. Anthrax toxin consists of three proteins called protective antigen, edema factor, and lethal factor.

There are 3 forms of the disease: cutaneous, inhalation, and gastrointestinal which occur when endospores enter the body through breaks in the skin or by inhalation or ingestion, respectively. Cutaneous anthrax accounts for the majority of the cases (95%). It is natural to expect that uncovered parts suffer the most severely. Head accounts for 44.6%, neck 31.2%, upper extremity 20.4% and lower extermity and trunk for 1.9% each[2]. The site of the lesion will depend on the nature of job. The case fatality of cutaneous anthrax depends largely upon the site of infection and the day treatment is started. It ranges from about 3% on the forehead to about 24% on the neck. Usual case fatality estimated is 5-15%. Respiratory and alimentary anthrax are almost invariably fatal. The incubation period of anthrax is usually short. In respiratory anthrax it is not more than 24 hours and in malignant pustule a lesion is evident within two days. Febrile patients with acute neurologic deterioration should be watched for rapidly fatal hemorrhagic meningoencephalitis.

The diagnosis is made as a result of typical clinical lesions, direct microscopy or bacterial isolation. Bacillus anthracis is susceptible to a number of antibiotics, including pencillin, erythromycin, tetracyclines, cephalosporins etc. It can be prevented by vaccination of the livestock and susceptible individuals. When diagnosed early enough and treated with the proper care, cutaneous anthrax is not a life-threatening disease. The challenge to today's dermatologic clinicians is simply to be prepared for recognizing it and not mistaking it for an insect bite.

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EFFECT OF FLUORIDE IONS ON THE ADERNAL GLANDS OF GUINEA PIGS

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The environmental pollution is a dangerous problem in the whole of world, one of the most complex health hazards resulting from the flourides. The disorder not only effect the harder tissues of the body but also have cumulative action of flouride products on soft tissues.

Solmann[1] studied the effect of chronic intoxication of sodium flurode on Adrenal glands of Albino rats and observes no specific changes histologically.

Daenesely[2] experimentally produced hypertrophy of adrenal cortex by imposing stress in absence of sodium fluoride administration.

Blexter[3] made both physiological and pathological studies of adrenal and thyroid glands of dogs after receiving fluorine. No change in adrenals were detected by him

Roholm[4] could not find any structural changes in the adrenal cortex.

Ogilivie[5] studied both acute and chronic fluoride intoxication. The adrenal cytology both critical and medullary,however, remained normal.

Prulson and Ericeson[6] in pilot study on rats found no pathology of liver, spleen and adrenals. Following chronic toxicity of sodium monofluoride with slight dose of flourides, the renal histological changes were characterised by the dictation of hanles loop, mostly in the outer part of the medulla and the interior part of the cortex. The interstitial inflammation was more pronounced with fibrosis.

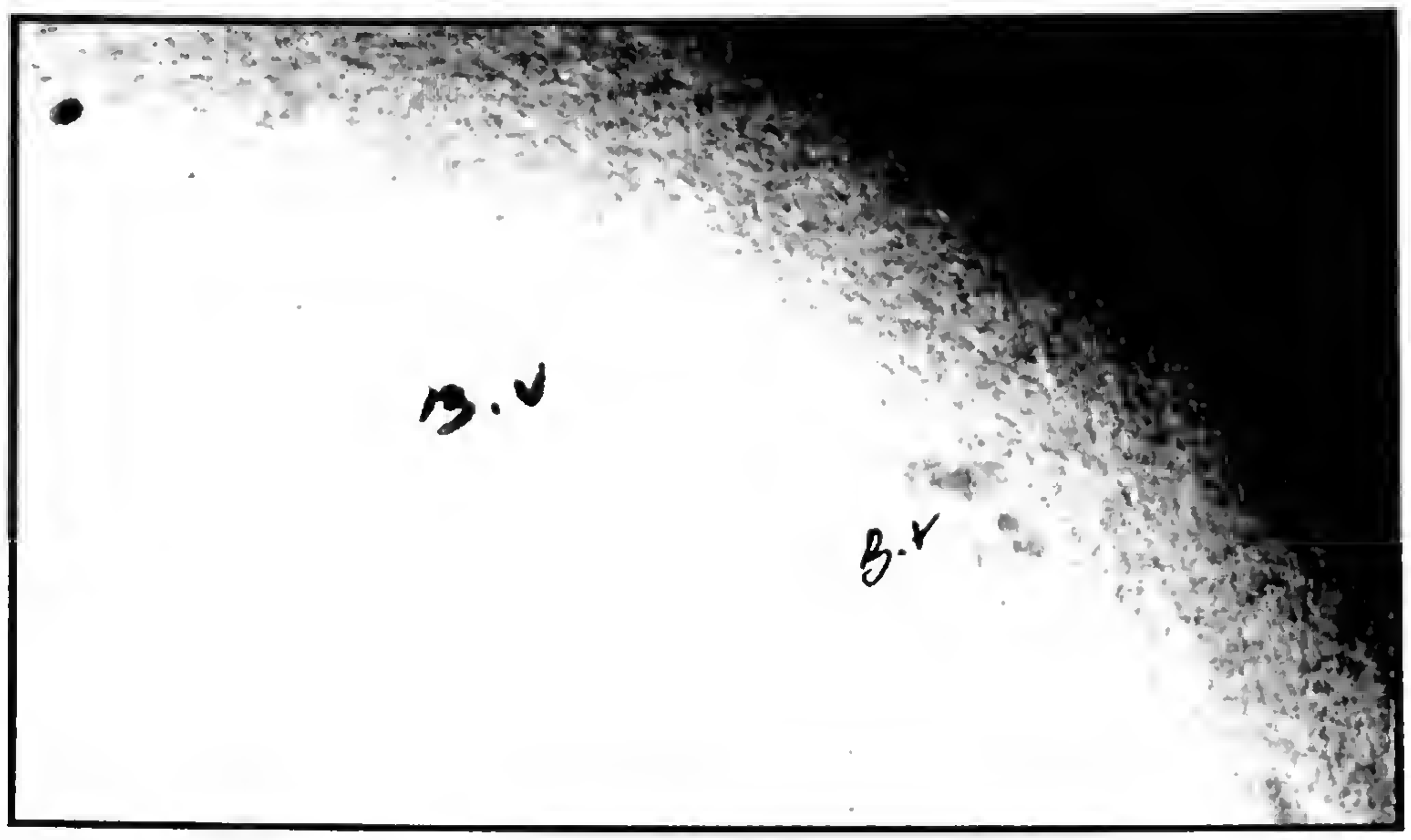

Fig-1

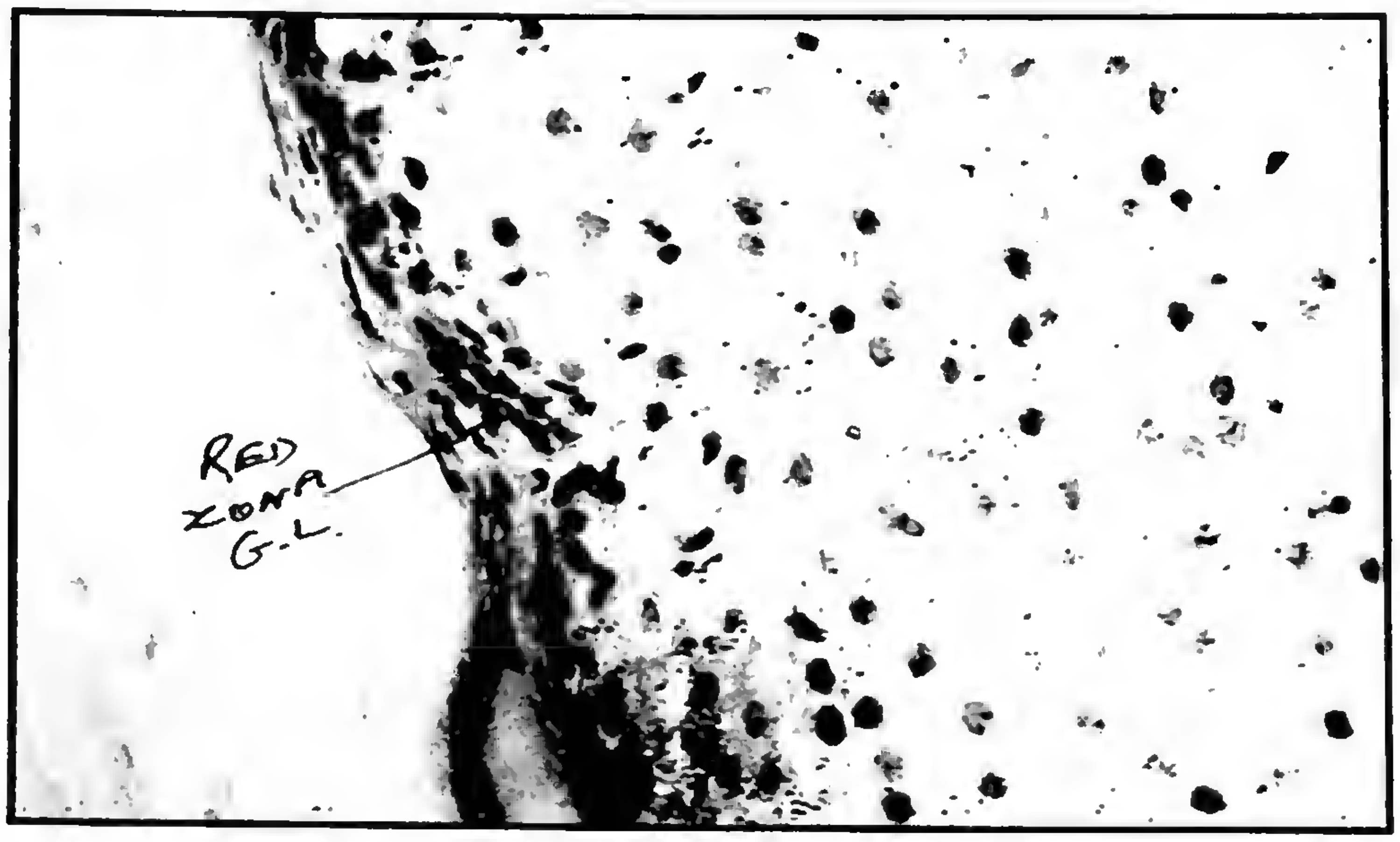

Fig-2

Denicoal[7] reported effect of sodium fluoride on the adrenal function in male rats. The concentration 0.02mg percent for 1-2 weeks did not have any effect.

In the present study, a total of 100 guinea pigs were taken and divided into four groups of 25 each. Group (A) was given drinking water containing 10 ppm of sodium fluoride in one litre of water. The group (B) was given 500 ppm of sodium fluoride in one litre of water. The group (C) was given 1000 ppm of sodium fluoride in one litre of water. The group (D) served as control. The group

A, B, C and D were fed on standard diet. The animals were observed for changes in gross appearance and body weight. The control and experimental animals were killed after 30, 60 and 90 days. The adrenal specimens obtained were processed for histopathological examination. Staining was performed by haemantoxylin and eosin stain.

OBSERVATION:

Adrenal Gland

Group (A) served no changes in the zone glomerulosa. Zone fasciculata and Zona reticularis. The meduilla showed no specific histological changes. The inter cellular connected tissue and blood supply were normal in all zones. There were no changes in the adrenal gland except a slight increase in its vascularity. The group (A) showed increased focal vascularity of the zona fasciculata. No other changers were apparent. (Fig. 1)

In group (B), the adrenal gland under microscopic examination showed slight odema of the cells in zona glomerulosa. The vascularity was however, increased. The group (B) also showed slight odema of the cells of zona glomerulosa. No other significant observation was recorded in this group. The group (B) showed focal area of degeneration in the zona glomerulos. The cells of the zona fasciculata were found slightly oedamatous. There was marked increase invascularity in zona glomerulosa and fasciculata (Fig. 2).

In group (C) the gland showed reduction in the zona glomerulosa. The vascularity was however, increased (Fig. 3). The group (C) on microscopic examination revealed reduction of zona glomerulosa. The other zones showed no remarkable changes. There was increased vascularity as compared to above groups. The group (C) on microscopic examination showed reduction of zona glomerilosa. The cells were formed swollen. No change was found in other zones. The vascularity was more increased (Fig. 4)

The adrena glands of the gunea pigs of group D showed normal zone glomerulosa zona fasciculata and reticularis. The glomerulosa cells were arranged in clumps with either oval or cricular nuclei. The zona Fasciculate were arranged as columns of polyhdral cells. The cytopism ws vasculated with circular nuclei. Zona reticularis exhibited network of polyhedral cells (Fig.5,6)

DISCUSSION

In the present study, the control group showed normal pattern. In the experimentally induced fluorosis with the strength of 500 and 1000 ppm, the cells of the zona fasciculata were found oedematous but the zona glomerulosa was reduced in size. However, the gland showed increased focal vascularity in zona fasciculata. The adrenal cortex known to be sensitive to conditions involving acute stress.

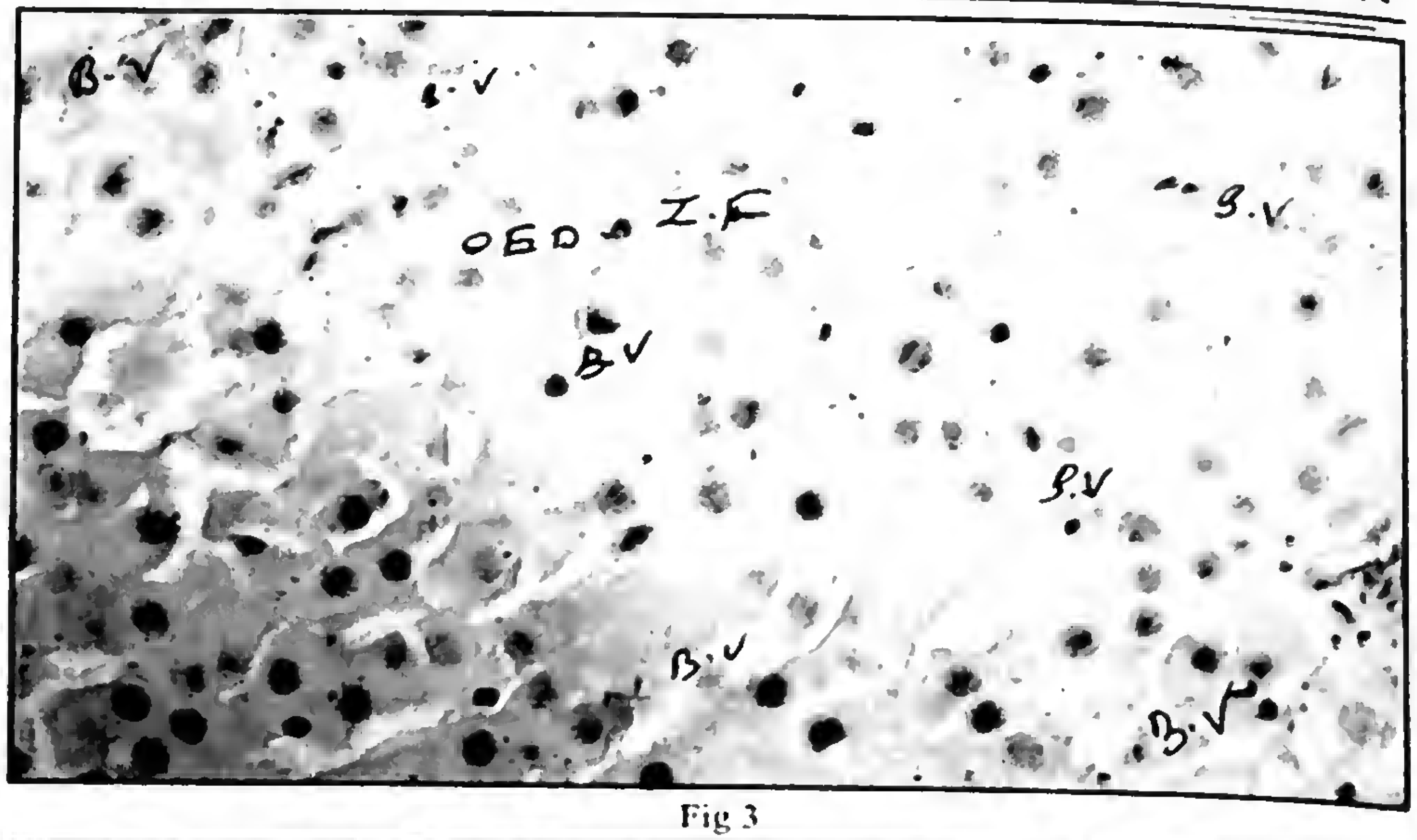

Fig 3

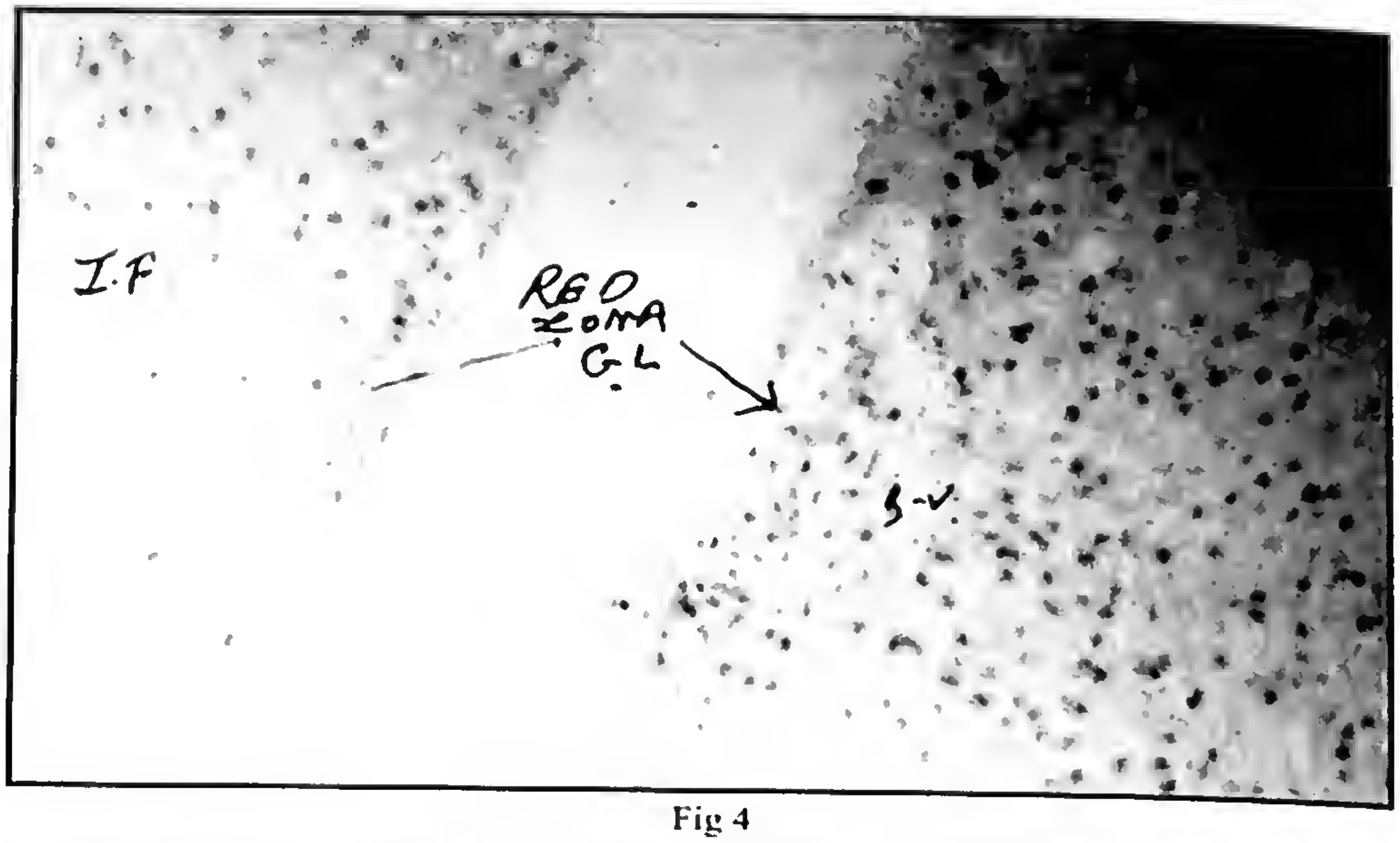

Fig 4

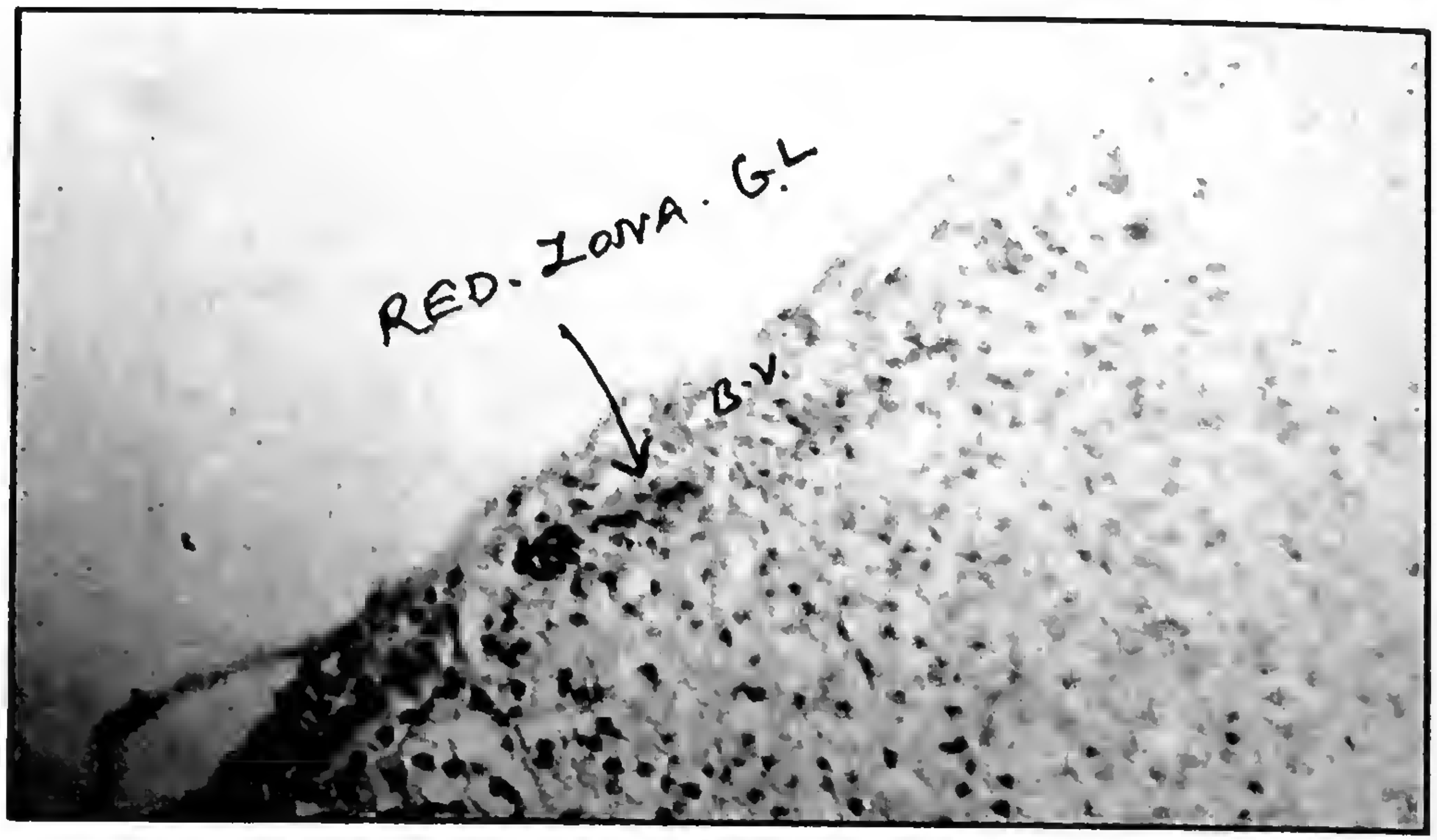

Fig 5

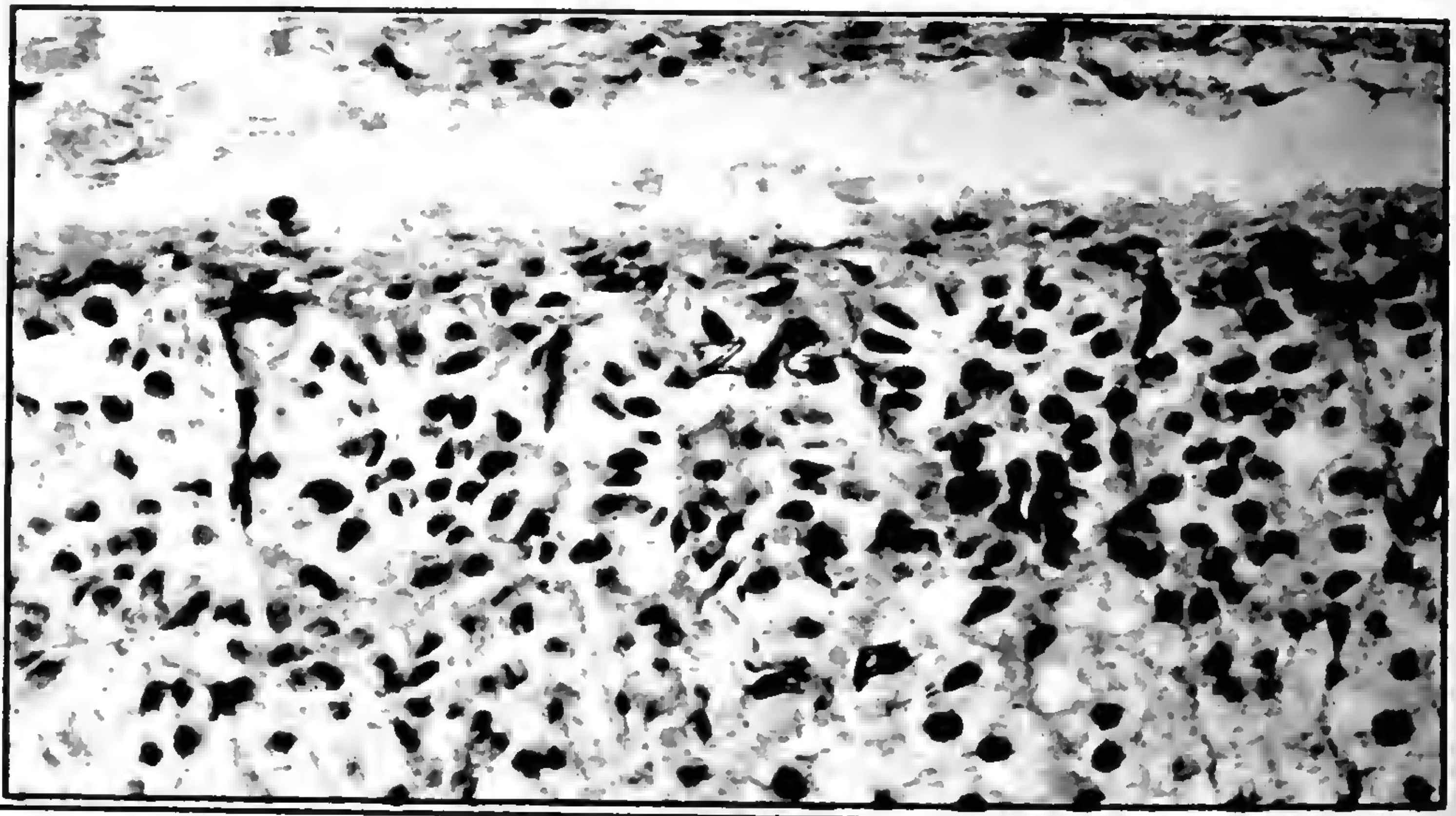

Fig 6

Daenesely[2] produced adrenal cortical hypertrophy by imposing experimental stress. Under such circumstances marked decrease in stainable lipids of the cortex was noticed. The changes in the adrenal lipids were not undertaken in the present investigation.

Ogilivie[5] demonstrated increased adrenal weight and cortical hypertrophy in acute fluorosis. The finding is identical with the work taken by Philips and co-workers (934), who also found hypertrophy and degenerative changes. However, chronic toxicity the adrenal cytology of the cortex and medulla was of normal configuration.

In contradiction, Solomann[1], Biesters[3] Rohlolm[4] and Poulsen[5] detected no alteration in adrenal glands following fluorine administration. Denicola[7] conducted an experimental study and reported only the biochemical changes in the adrenal glands in male rats with fluorosis. They made no mention about histological changes.

Poulsen[6] while studying the effect of sodium monofluoric phosphate could not detect any histological changes in the experimental animals.

SUMMARY AND CONCLUSIONS

With the administration of sodium fluoride in low concentration the[1] zona glomerulosa was found reduced in size.[2] Zona fasciculata exhibited odematous changes associated with increased focal vascularity.

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ENDOPHTHALMITIS PROPHYLAXIS IN CATARACT SURGERY

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The term endophthalmitis refers to intraocular inflammation predominantly involving the vitreous cavity and anterior chamber of the eye. Infectious endophthalmitis, inflammation associated with an infectious process is the most common form. Classically, most cases of infectious endophthalmitis develop after intraocular surgery. There are more than 2 million cataract surgeries performed each year in the United States. Fortunately, the incidence of postoperative endophthalmitis is relatively low, with an estimated five to ten cases per 10,000[1,2]. Overall, the incidence of post operative endophthalmitis for cataract surgery by extracapocilar cataract extraction or phacoemulsification ranges between 0.07% and 0.12%. When endophthalmitis occurs, the outcome for the patient can be devastating. As such, there is much interest and need in minimizing the occurrence of endophthalmitis. There are few well-controlled studies of the risk factors or efficacy of preventive measures because of the low incidence of this condition. Pre-operative disinfection of the surgical site and meticulous attention to sterile technique are essential. The role played by perioperative antibiotics is uncertain.

Phage typing and DNA fingerprint analysis have shown that the organisms that cause postoperative endophthalmitis, despite their low virulence in other surgical settings, are those.that reside on the patient's own lid flora and adnexa[3,4]. Staphylococcus epidermidis is the most common infecting bacteria, followed by staphylococcus aureus and rarely, gram negative rods or even candida. Staphylococci bacteria are ubiquitous and S.epidermidis is considered normal flora on the skin and lid.

In the operating room, it is imperative to have a "Sterile technique" but it is not uncommon for the anterior segment to become contaminated during cataract surgery. Reports suggest that bacteria can be isolated from anterior chamber fluid upto 43% of the time following cataract surgery[5]. Despite this, endophthalmitis is still a rare occurrence. It appears that there may be a threshold inoculum necessary to cause endophthalmitis.

STRATEGY:

Given that the majority of organisms come from the patient's own flora, the most practical way to decrease the potential inoculum is to decrease the number of organisms on the lid margin or in the cul-de-sac. This can be effectively done using povidone-iodine, such as Betadine or povidone-iodine plus antibiotics. Povidone-iodine 5% has been shown to significantly decrease the incidence of endophthalmitis and is effective in reducing the number of organisms in the cul-de-sac[6,7].

Povidone-iodine releases free iodine, which kills organisms via oxidation. As an oxidizing agent, it requires time for killing; in vitro experiments suggest 1 to 2 minutes of contact time. It is advised to prepare the lid margin skin and place 5%. Betadine directly into the cul-de-sac so that it has at least 1 to 2 minutes of contact time with the tissue. More dilute povidone-iodine solutions have adequate amounts of free iodine and are also effective; however, the less concentrated solutions are not as stable and must be made up fresh.

Preoperative antibiotics have been advocated in addition to using preoperative Betadine because antibiotics further decrease the number of organisms, both on the lid margins and in the cul-de-sac[8,9,10]. There are no controlled prospective studies that prove a decrease in the incidence of endophthalmitis with the use of preoperative antibiotics.

Preoperative antibiotics have little intrinsic risk. The choice of antibiotic is most likely more controversial. The ideal antibiotic would have broad spectrum, would be nontoxic and would have a fast killing time. Using these criteria, the fluoroquinolones would be the best choice.

Among the fluoroquinolones, both ciprofloxacin HCL and Ofloxacin have been shown to have comparable spectrums of activity[11] and comparable kill times[12] and are both relatively safe. Because Ofloxacin is more soluble (pH 7.0), it has better tissue penetration[13]. Aggressive dosing of Ofloxacin (1 drop every 5 minutes five times preoperatively) can yield approximately 1 mm of Ofloxacin per milliliter of aqueous[14]. Similar unpublished studies show results with 2 drops every 30 minutes two times. This is above the minimum inhibitory concentration (MIC) for many strains of S.epidermidis. Therefore Ofloxacin is more favourable than Ciprofloxacin. Levofloxacin is the L-isomer of Ofloxacin. It may have more favourable MIC levels and attain higher tissue penetration, although the safety of the formulation has not been reported with regard to epithelial would healing.

There are other measures that are generally accepted and recommended to reduce the inoculum. It has been traditionally advocated and is important to identify patients with active blepharitis, treat them and avoid intraocular surgery until their lid disease is controlled. Daily lid scrubs with an adjunctive antibiotic or antibiotic/steroid ointment to the lids at bed time can be effective. In cases with concomitant ocular rosacea, tetracycline 250 mg four times a day for 1 month or doxycycline 100mg/day will help control the meibomianitis. Additionally, isolation of the lids with adhesive tape or plastic tape dressings is recommended. This prevents meibomian secretions or debris surrounding the hair follicles from contacting the surgical site.

Table: Recommendations for preventing endophthalmitis.

- Identify and treat preoperative blepharitis
- Reduce inoculum. Preoperative antibiotic Ofloxacin four times a day start 1 day preoperatively.
- Betadine 5% to cul-de-sac, lids and skin 2 minutes contact as a preoperative preparation.
- Isolate the lids
- Although most cases of endophthalmitis arise from the host flora other sources are also important.
- Avoid prolene haptics
- Administer postoperative topical antibiotics unitl the epithelium is healed
- Consider oral Ofloxacin for special cases in which the risk is high.

The role of intraoperative antibiotics remains controversial. A number of investigators have suggested that aminoglycoside and vancomycin used intracamerally, or vancomycin alone, injected in the bag can significantly reduce the risk of endophthalmitis[15, 16]. A survey conducted by the American Society for Cataract and Refractive Surgeons has shown at least 35% of Ophthalmic surgeons currently use intracameral antibiotics. Vancomycin was used by 80% and gentamicin by more than 40% of the surgeons surveyed[17]. Although the anecdotal and retrospective analyses are appealing and show that the relative risk of endophthalmitis is reduced, there is no solid prospective evidence in the peer-reviewed literature to support this practice. Additionally, there is some potential for causing toxicity. Gentamicin has a narrow therapeutic safety range and significant retinal toxicity can occur above 100 mm/cc, while vancomycin can cause cystoid macular edema.

Vancomycin injected at 20 mm/cc has been shown to have a half life of approximately 2 hours, which is relatively short. This is important because vancomycin is relatively slow at killing organisms. Intracameral antibiotics may be appropriate; however vancomycin does not appear to be the right choice. Ferro and colleagues showed that adding vancomycin and gentamicin did not statistically reduce the number of anterior segment aspirates that were positive for bacteria following cataract surgery[18].

Vancomycin requires actively growing bacteria to be effective and will not work unless the bacteria are in active phase. In lieu of vancomycin, one would more likely benefit from having an antibiotic that is fast killing, has broad-spectrum killing of both gram-negative and gram-positive organisms and one in which the antibiotic concentration can be augmented and maintained with supplemented topical antibiotics. In the future, perhaps a fluoroquinolone antibiotic with these preferred requirements will be found to be useful.

Postoperative subconjunctival injections of antibiotic have also been practiced for many years. The benefit could come from delivery of therapeutic levels of antibiotic to the anterior chamber, which would result in the reduction of bacteria numbers and prevent clinically significant endophthalmitis. In prospective studies, Christy was not able to show a benefit from subconjunctival antibiotic alone, but did have a benefit from subconjunctival plus preoperative topical antibiotic. More recent retrospective analysis by Colleaux and Hamilton revealed a statistically significant reduction in the incidence of endophthalmitis when subconjunctival antibiotics were used[19].

Gentamicin is toxic to the retina and there is significant concern among retina surgeons as to the safety of routine postoperative injections of gentamicin[20]. Cefazolin alone has not been established as effective in scientific studies. However, subconjunctival injection of Cefazolin is probably much safer and deserves further evaluation. With the trend towards clear cornea and topical or intracameral anesthetic, the use of subconjunctival injection is less practical.

Postoperatively, endophthalmitis can still occur via contamination of the anterior segment while the wound is still open. This may be a problem with clear cornea and topical anesthesia, or even scleral wound incisions that may gape and take contaminated fluid back into the eye. Because of this, continued antibiotic therapy is advised until the epithelial barrier has been established. The ideal choice of antibiotic would again be one with broad spectrum, fast-acting, relatively high solubility and relatively sustained tear film levels with low toxicity. Again, the fluoroquinolones are the best choice. Ofloxacin is the most favourable choice because it has the best solubility at pH7, relatively good penetration and persists in the tear film for relatively long periods of time Levofloxacin may prove to be superior, however, toxicity studies remain to be completed.

Attention to adequate wound closure is also important. It is recommended to check the wound with fluorescein when the case is over, injecting balanced salt solution into the stroma to enhance the seal if necessary or placing a suture if there is persistent leakage or if the patient is expected to have compromised wound healing.

Prolene haptics can increase the risk of endophthalmitis by approximately 4 - 5 times[21]. This is due to ability of Staphylococcus to directly bind to prolene. The elimination of prolene haptics may be necessary to maximally reduce the risk of endophthalmitis. Additionally, a surgeon should avoid directly contaminating the IOL by not placing it on the eye or touching it to the lid margins.

In the report of MeniKoff and colleagues, the highest risk for endophthalmitis (14 times) occurred with capsule rupture[21]. In such high risk cases, the addition of antibiotics that reach therapeutic levels in the vitreous may be appropriate. Subconjunctival antibiotics are generally not believed to reach high enough vitreous levels[22]. Systemic antibiotics have not been traditionally found to effectively cross the blood-aqueous barrier. More recently, the fluoroquinolones have been found to penetrate the eye well because of their increased lipid solubility. Ofloxacin seems to be approximately two times better than Ciprofloxacin[23]. Oral Ofloxacin 400mg twice a day in conjunction with topical Ofloxacin has been shown to reach a concentration of approximately 2.7 mm/cc in the aqueous[24]. In the higher risk cases, the addition of systemic Ofloxacin 400 mg twice daily for 3 days, with 2 days of topical Ofloxacin 0.3% every 2 hours is recommended. This regimen should not be adapted to all cases because of the risk of increased resistance to fluoroquinolones and increased medical costs.

Sterile technique is an important prevention method. This includes following manufacturer's recommendation regarding sterilization and use of disposables. Excessive talking and coughing have been implicated as not being sterile in repeated cases and should be kept to a minimum.

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PSYCHOLOGICAL ASPECTS OF SKIN DISEASES: AN OVERVIEW

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The mysteries that lie behind veiled eyes foretell the drama of life.The thoughts that spring in the deepest recesses of our mind and guide our actions, our behavior and our responses still remain an enigma.

Beyond the realms of understanding, lies a wide field,unexplored and ill-defined-that of our psyche.Perhaps ,the uncertainties of so many skin disorders are rivaled only by the uncertainties of the individual's psyche and the pertinence of each on the other.

The psychological aspect of skin diseases has been recognized by laymen as well as researchers[1].Broadly divided into three major categories,the psychocutaneous disorders are considered as:

I. Psychiatric Disorders Expressed in the Skin
- **A. Delusions and Hallucinations**
  - 1. Delusions of parasitosis
  - 2. Dysmorphic delusions and hallucinations
- **B. Factitious Syndromes**
- **C. Obsessional Concerns**
  - Body dysmorphic disorder.
- **D. Compulsive Habits**
  - 1. Trichotillomania
  - 2. Neurotic excoriations.
  - 3. Less common examples

II. Dermatological Disorders with A Psychophysiologic Component
- **A. Psychogenicpruritus**
- **B. Chronic Urticaria**
- **C. Psychogenic Purpura Syndrome**
- **D. Alopecia Areata**
- **E. Telogeneffluvium**
- **F. Typical Pain Syndrome**
- **G. Chronic Inflammatory Dermatosis**

III. Somatopsychic reactions

Out of these group of disorders,dermatological disorders with a psychophysiological component are the most relevant to the present discussion.

It is known that emotional stress can induce or exacerbate a severe episode of psoriasis as also delay its resolution[2,3] In recalcitrant chronic atopiceczema of childhood, the role of impaired parent-child relationship is recognised[4].An auto-immune disease like pemphigus has been seen to be triggered by stress.[5]In systemic lupus erythematosus,stress has been seen to increase the severity of nephritis but on the contrary, decrease the severity of arthritis.

The successful treatment of warts by various modalities including hypnosis is obviously dependent upon the personality traits of the patient. An increased susceptibility to bacterial and fungal infections is seen to occur in mentally disturbed patients.[6] The number of recurrences of herpes progenitalis and herpes labialis in a patient is dependent upon the stress and loneliness to which he/she is exposed[7]. A poorly understood disorder like chronic urticaria has a link to life events and psychological stress. Experiments on rodents show that wound healing is delayed in patients under stressful circumstances[8]. Rosacea is known to be triggered by anger.Stress has been linked to a faster progression to Acquired Immunodeficiency syndrome[9]. In addition, psychogenic pruritus, psychogenic purpura and alopecia areata are influenced by stress. As a further corroborative evidence, modalities to reduce stress such as biofeedback, hypnosis, anxiolytics and social interventions have been tried in recalcitrant skin disorders with favourable results.[10] A randomized controlled study of patients with melanoma showed improvement in those treated with psychological interventions[11]. Various anti-stress modalities such as hypnosis, biofeedback, meditation and relaxation techniques have been tried with success in patients with vitiligo and psoriasis.

These studies reveal beyond an iota of doubt that skin diseaes can be induced,exacerbated or prolonged by stress.The relative importance however, varies from individual to individual depending upon the person.s perception of a particular situation as stressful and his/her emotional maturity in handling it.

Now the question arises how does stress affect skin disease? Scientific research has proved in concrete terms that psychological aspects of skin disease is not old wives, tales.In an interesting study, Garg et al showed that there is a decline in the permeability barrier recovery kinetics after barrier disruption by cellophane tape stripping in parallel with an increase in the perceived psychological stress during high-stress occasions[12].This suggests that stress-induced derangements in epidermal functions act as precipitators of inflammatory dermatoses.No matter how diverse the precipitant .stress is perceived by the hypothalamus as a unique stimulus.The paraventricular nucleus releases corticotropin releasing factor. This acts on the pituitary to release ACTH inducing the release of adrenal gluco-corticoids[13].Activation of the adrenergic locus ceruleus system results in a surge of norepinephrine into the blood.Both the gluco-corticoids and catecholamines modify the immune response by causing preferential activation of the Th-1(humoral immunity) helper cells through Interleukin (IL)-4. IL-5. IL-10 and the suppression of Th-1(cell mediated immunity) cytokine response[14-16].This results in the exacerbation of all those diseases where humoral Th-2 responses predominate such as atopic eczema and lupus nephritis.Evidence for this is provided by the following observations:

1) in both rodents and humans, stress caused endogenous glucocorticoid production[18].

2) Steroids adversely affect barrier homoestasis and epidermal cell proliferation[17-18].

3) co-administration of steroid hormone receptor antagonist RU-486 along with psychological stressors blocks the development of barrier abnormality.[18]

In addition to glucocorticoids,neuropeptides play a pathogenetic role.[19] Descending autonomic nerve signals could antidromically release neuropeptides like substance P and vaso-active intestinal peptide in the skin.Both these neuropeptides are keratinocyte mitogens and their levels are increased in the involved skin of patients with psoriasis and atopic eczema.These neuropeptides and other cytokines could change the threshold for physical insults (Koebner's phenomenon) or prolong recovery from insults resulting in decreased threshold for disease induction.

The positive fall-out of these observations is that they add to the dermatologists, armamentarium against skin diseases.Modalities like biofeedback training, behavioural therapy, calcitonin gene related peptide, anxiolytics, melanotropins, corticotrophin releasing factor receptor antagonists, blockers and others could provide us with novel interventions in patients with dermatological diseases by inhibiting the effect of stress on skin.

To conclude,emotions rule the world and the skin is no exception.For a healthy attitude towards life and a positive body image the psyche of skin should not be ignored.

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FINE NEEDLE ASPIRATION CYTOLOGY OF "THYROID NEOPLASMS" A TEN YEAR (1993-2003) STUDY BASED ON 400 NEOPLASMS.

A.R.Khan, Syed Besina Yasin, Rumana Makhdoomi, Seema Ali Bhat

ABSTRACT

A 10 year review of FNA revealed 2888 thyroid lesions,2330 non-neoplastic,400 neoplastic & 158 inconclusive cases.Neoplastic lesions included 210 Follicular & Follicular related neoplasms,141 Papillary carcinomas , 13 Medullary carcinomas,12 Undifferentiated carcinomas, 15 Primary non-Hodgkin's lymphoma & 9 metastatic non-lymphoid malignances.Out of 210 Follicular & Follicular related neoplasms,including 182 Follicular neoplasms,1Hyalinising trabecular adenoma,18 Hurthle cell neoplasms & 9 follicular carcinomas histopathology for comparison was available for 65 cases of Follicular neoplasms,18 cases of Hurthle cell neoplasms & 9cases of Follicular carcinomas diagnosed on FNA. Histology of 65 Follicular neoplasms revealed Follicular adenoma in 55 cases,follicular carcinoma in 7cases & hyperplastic goitres in 3 cases accounting for false positive cases & overall sensitivity of 65%.Out of 18 cases of Hurthle cell neoplasms,15 proved Hurthle cell adenomas & 3 as Hurthle cell carcinomas.9 follicular carcinomas were interpreted as such,2of these had bone metastasis.

Out of 141 Papillary carcinomas,134 were correctly diagnosed including 12 cases of cystic papillary carcinomas & sensitivity of 96.4%.7cases diagnosed incorrectly included 1 case of suspicious papillary carcinoma which proved to be follicular adenoma;4cases of follicular variant of papillary carcinoma interpreted as follicular neoplasm,1case of papillary carcinoma with marked Hurthle cell metaplasia interpreted as Hurthle cell neoplasm & 1case of cystic papillary carcinoma in the neck interpreted as hemangioma.Overall there were 13cases of cystic papillary carcinoma out of which 12 were correctly interpreted.Out of 13 cases of medullary carcinoma 11 were correctly interpreted,1diagnosed as undifferentiated carcinoma & another case diagnosed as follicular adenoma.The last 2 cases were undifferentiated small cell carcinoma on histopathology & required immunohistochemistry for confirmation.12 cases of undifferentiated carcinoma were correctly interpreted .15 cases of primary non-Hodgkin's lymphoma were diagnosed on FNA-14 of large cell type and1 of low grade MALT type. Histopathology was available only in 2cases from incisional biopsy to confirm the diagnosis.These lymphomas were stage I/II tumours,all treated with good response in all the cases.9 cases of metastatic cancers,all known cases of cancer.(Oesophageal 7,6 squamous & 1 adeno,laryngeal-2 both squamous).

In summary,sensitivity & specificity of papillary, medullary,undifferentiated carcinomas & primary NHL is very high.In follicular category,apart from inability to distinguish between follicular carcinoma & adenoma,the problem arises from hyperplastic colloid nodules with & without degeneration & in follicular neoplasms with cystic degeneration.Both sensitivity & specificity of FNAC of thyroid neoplasms increases with experience.

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INTRODUCTION

Fine needle aspiration (FNA) is a well accepted procedure for both neoplastic & non-neoplastic diseases of thyroid, both nodular & diffuse. It is the single most accurate diagnostic modality than other combination of tests available in the investigation of solitary thyroid nodules.[1-3] Risk of nodules palpable during life varies from 5-10% of surgically excised nodules & 5-15% of these prove to be malignant[4]. FNA diagnosis of benign diseases will exclude surgery or limited surgery in benign,potentially malignant neoplasm & definite treatment for malignant lesions like Papillary, Medullary & Undifferentiated carcinomas & Primary lymphomas of thyroid. In fact goal of the procedure is to identify lesions for medical therapy and surgery. The limitations are false negative and false positive rate of malignancies. False negative of 5-10% in the hands of experienced cytopathologist excluding occult type of cancer[5]. (Lowhagen 1979). False negative results stem from cystic lesions,geographical misses (in small tumours especially occult type) dual pathology & errors in interpretation[6-9]. (Hamburger 1986[6], Hsu 1987[7].

The false positive rate is low accounting for 1-3% of malignancies.[1]

Aspiration can be attempted by cytopathologists or clinicians, but we prefer cytopathologists. Procedure can be attempted directly in large & palpable lesions. In small or missed lesions the diagnostic accuracy can be increased by USG, radionucleid scanning & USG guided FNA.

Key words: Words: Follicular neoplasm, Papillary carcinoma, Medullary carcinoma & Undifferentiated carcinoma, Primary NHL, Metastatic cancer.

The authors review and report 10 years FNAC experience of thyroid neoplasms.

MATERIAL & METHODS

2888 cases of thyroid disorders were subjected to FNA over a period of 10 years(1993-2003). One of us (ARK) was the chief aspirator and interpretor. Aspiration was conducted mostly by conventional methods. Some haemorrhagic aspirations were done by non-aspirator technique. In the conventional method patients were placed supine with a pillow under the neck and advised not to swallow at the time of needle insertion. 10-20 ml disposable plastic syringes with or without syringe holder were used with 22 or 24 guage disposable needles. 2 -4 passes were made in each case and material spread on 4 - 8 slides. MGG was the main stain used for interpretation supplemented with haematoxylin & eosin in some cases. 1 - 2 slides were fixed in alcohol & reserved for any special stains.

RESULTS

Over a period of 10 years (1993-2003) 2888 thyroid lesions reviewed & analysed revealed 2330 non-neoplastic & 400 neoplastic lesions & there were 158 inconclusive cases (Table I-III). Neoplastic lesions (Table IV)included 210 Follicular & related neoplasms, 141 Papillary carcinomas, 13 Medullary carcinomas, 12 Undifferentiated, 15 Primary non-Hodgkin's lymphoma & 09 Metastatic cancers. Final analyses of FNA & Histopathology revealed 209 cancers (Table V) constituting 52.5% of all lesions.

Follicular Neoplasms & Variants (Table VI)on FNA were divided into 4 categories. Category 1 included Follicular neoplasms-141 cases .Follicular neoplasm/Hyperplastic colloid nodules - 40cases & 1case suspicious/suggestive of Papillary carcinoma. Histopathology available in 60cases of follicular neoplasm revealed follicular neoplasm-51cases, follicular carcinoma-7cases & colloid goitre-2cases. Histopathology available only in 4 cases of follicular neoplasm/hyperplastic colloid nodule revealed follicular adenoma in 3 & colloid goitre in 1 case. 1case suspected of papillary carcinoma, because of frequent intranuclear vacuolations as the only dependable criterion, revealed follicular adenoma on histopathology.

No histopathology for comparison was available in case of hyalinising trabecular adenoma. 18 cases of Hurthle cell neoplasm revealed Hurthle cell adenoma in 15 cases and Hurthle cell carcinoma in 3cases. 9 cases of Follicular carcinoma diagnosed clinically and on FNA smears were confirmed as such on histopathology. 2 of these had bone metastasis.

Papillary Carcinoma

Table VII & VIII show that there were a total of 141 tumours diagnosed on FNA with 102 cases from thyroid, 12 cases from thyroid + lymph nodes & 27 cases from cervical lymph nodes. All the patients had histopathology for comparison. FNAC diagnosis included Papillary carcinoma in134 cases, Follicular neoplasm in 4 cases, Hurthle cell neoplasm in 1 case & hemangioma 1 case. 4 cases of follicular neoplasm also proved to be papillary carcinoma of follicular type (2 cases)&mixed papillary-follicular carcinoma (2cases) on histopathology.

The case of Hurthle cell neoplasm proved to be papillary carcinoma with Hurthle cell metaplasia. Out of 13 cases of cystic papillary carcinoma 12 were correctly interpreted on FNA. 1case presenting as a swelling neck yielded hemorrhagic fluid & was labelled as hemangioma .

Table -I

FNAC — Thyroid

Diagnosis	No.of Cases
1. Non-neoplastic	2330
2. Neoplastic	400
3. Inconclusive	158
Total	2888

TABLE - II

FNAC — Thyroid (Non-neoplastic)

Diagnosis	No.of Cases
1. Goitre (Parenchymatous nodular,cystic)	1906
2. Thyroiditis	340
3. Thyroglossal cyst	82
4. Ectopic thyroid	02
Total	2330

TABLE - III

FNAC — Thyroid

THYROIDITIS

Diagnosis	No.of Cases
1. Acute thyroiditis	08
2. Tuberculous thyroiditis	11
3. Subacute thyroiditis	142
4. Chronic lymphocytic (Hashimoto's)	179
Total	340

TABLE - IV

FNAC — Thyroid

Neoplastic Lesions

Diagnosis	No.of Cases
1. Follicular	210
a) Follicular neoplasm	182
b) Follicular carcinoma	09
c) Hurthle cell neoplasm	18
d) Hyalinising trabecular adenoma	01
2. Papillary carcinoma	141
3. Medullary carcinoma	13
4. Undifferentiated carcinoma	12
5. Non-Hodgkin's lymphoma	15
6. Metastatic	09
Total	190

TABLE - V

FNAC — Thyroid

Primary malignancy

Diagnosis (FNA/Histopath.)	No.of Cases
1. Follicular carcinoma	16
2. Hurthle cell carcinoma	03
3. Papillary carcinoma	141
4. Medullary carcinoma	13
5. Undifferentiated carcinoma	12
6. Non-Hodgkin's lymphoma	15
7. Metastatic	09
Total	209

Medullary Carcinoma

Table IX shows that there were 13 cases of medullary carcinoma. 11 of these were correctly diagnosed as medullary carcinoma. 1 case as small cell anaplastic carcinoma & 1case as follicular neoplasm. The last 2 cases proved undifferentiated small cell carcinoma on histopathology and required immuno histochemistry & tumour cells were immunoreactive with calcitonin, CK & CEA.

Undifferentiated Carcinoma

Table X shows that there were 12 cases of undifferentiated carcinoma. 2 of these tumours were complicating long standing colloid nodular goitres. Histopathology available in all cases confirmed the FNA diagnosis .

Non-hodgkinslymphoma

As seen in table XI there were 15 cases of primary non-Hodgkins lymphoma,on FNA 14 were labelled as large cell lymphoma and 1case as low grade tumour. (MZL/Malt lymphoma). Histopathology from incisional biopsy was available in 2 cases,which confirmed the diagnosis of large cell lymphoma. One of these required immunohistochemistry for confirmation.

Metastatic malignancies

There were 9 cases of metastatic cancers .The cytological diagnosis was squamous cell carcinoma in 8 cases & adenocarcinoma 1 case.Since these were known cases of cancer (7 of esophagus-6 squamous &1 adeno and 2 of larynx-both squamous) there was no necessity to hunt for the primary.

CYTOLOGICAL CRITERIA

Follicular neoplasm:

Cytology of follicular neoplasm is well described[10-5]. Smears are generally moderately to highly cellular except in tumours with cystic degeneration.Tumours cells are larger than normal follicles with high N/C ratio, arranged in micro -follicles rosette-like structures without lumen ,syncytial & solid cell clusters &cell trabeculae.Scanty colloid is present in the background except in macrofollicular adenoma which produces cell sheets mimicking colloid goitre.Smears of follicular adenoma & well differentiated follicular carcinomas are indistinguishable. however some authors diagnose over 75% of follicular carcinomas on cytology[12,16]. These tumour cells have larger nuclei with prominent nucleoli, more coarse & irregular chromatin. Pleomorphism of tumour cells is a feature of atypical follicular adenoma rather than follicular carcinoma.Hurthle cell neoplasm including adenomas & carcinomas cannot be distinguished on cytology like follicular neoplasm. The ultimate behaviour in both follicular & Hurthle cell neoplasm is determined by vascular and/or capsular infiltration. Hurthle cells are larger cells with abundant pale granular cytoplasm. larger nuclei, one or more than one and with prominent nucleoli . (Fig.1-4)

Hyalinising trabecular adenoma show cytological features mimicking papillary & medullary carcinoma[17]. There is predominantly a dissociated population of round, oval, polygonal & spindle cells with pale blue cytoplasm & central or eccentric nuclei. The cells may show nuclear grooves ,intranuclear cytoplasmic vacuolations & even psammoma bodies. Hyaline stromal material is present. FNA smears are not diagnostic but at the most raise the diagnostic possibility.

TABLE-VI
FNAC —Thyroid
Follicular neoplasms & variants

FNA Diag.	No.of cases	Age-years	Sex F/M	Histopath.diag.	No.of cases
1.Follicular neoplasms	184	15-80	37/47	a)Follicular adenoma	55
				b)Follicular carcinoma	07
				c)Hyperplastic colloid goitre	03
2.Hyalinising trabecular adenoma.	01	17	0/1	x	x
3.Hurthle cell neoplasm	18	20-69	17/1	a)Hurthle cell adenoma	15
				b)Hurthle cell carcinoma	03
4.Follicular carcinoma	09	50-79	7/2	Follicular carcinoma	09

TABLE VII
FNAC----Thyroid (Neoplastic)
PAPILLARY CARCINOMA

Cytologic Diagnosis	No.of cases
1. Thyroid Neoplasm	102
2. Thyroid Neoplasm + cervical lymphadenopathy	12
5. Cervical nodes	27
Total	141

Cystic Papillary Carcinoma---13 cases.

Papillary carcinoma

Smears are moderate to highly cellular with papillary cell clusters, mono-layered sheets &psammoma bodies and chewing gum ropy colloid. Tumour cells are polygonal, cuboidal, spindle & cylindrical with distinct cell borders, dense cytoplasm[2], large nuclei with finely granular chromatin, intra-nuclear cytoplasmic inclusions & nuclear grooves are common. Also presnt are lymphocytes macrophages & foreign body giant cells. According to Miller et al [18] the most important parameter in predicting the diagnosis of papillary carcinoma are intranuclear inclusions ,papillary structures without vessels and metaplastic cytoplasm. Follicular, tall cell, oxyphilic and sclerosing types have been described. Excellent references are available on the subject.[19-24]. (Fig.6,7,8,9,10)

Medullary carcinoma

Cytologic description of typical &atypical tumours is available.[15,25-26].

Smears are moderately cellular with dissociated cell pattern, syncytial aggregates and less often follicular & papillary. Tumour cells are ovoid, polyhedral. triangular, plasmacytoid, spindle cells with scanty to abundant bluish cytoplasm with mono-bi-tri-& multinucleated cytoplasm. Some cells contain eosinophilic granules. Nuclear chromatin is finely granular with indistinct nucleoli. Nuclear vacuolations are occasionally seen. Fragments of extra cellular amorphous pale pink to violet material representing amyloid may be seen. Conventional & mixed tumours can be diagnosed on cytology alone. Pure atypical variants require immunohistochemical studies. (Fig.11,12,13)

Undifferentiated carcinoma

Cytology of these tumours has been described.[27-28]. Smears are cellular with pleomorphic malignant cytology with tumour diathesis including necrotic cell debris and inflammatory cells.Tumour cells include small cells & large cells with epithelial,spindle cell & giant cell types. (Fig.14)

Lymphomas

Cytologic criteria for nodal & extra nodal lympomas have been described.[29-30] Lymphomas are usually of B-cell lineage. Most of the lymphomas are of large cell type and less often of low grade MALT type .Large cell lymphomas are comparatively easy to diagnose compared to low grade lymphomas.(Fig.15)

Metastatic malignancies

Cytologic criteria of metastasis in thyroid are same as else where.Some metastastic tumours like renal cell carcinoma of clear cell morphology & medullary carcinomas & small cell anaplastic carcinoma mimic follicular & medullary carcinomas of thyroid respectively. In absence of history of extra-thyroid malignancy,immunohistochemistry may be required to differentiate between primary & metastatic cancer. (Fig.16)

DISCUSSION

Over a period of 10 years 2888 thyroid aspirations reviewed revealed 2330 non-neoplastic & 400 neoplastic lesions. Neoplastic lesions included 210 follicular lesions, 141 Papillary carcinomas, 13 Medullary carcinomas,12 Undifferentiated carcinomas,15 Primary NHL & 9 metastatic cancers.

Follicular & Related Neoplasms were divided into 4 categories.Category one included 141 follicular neoplasms on FNAC with histopathology available in 65 cases ,revealed follicular neoplasm in 55 cases ,follicular carcinoma in 7 cases & colloid goitre in 3 cases.Thus there were 3 cases of false positive diagnosis of follicular adenoma for colloid goitre. There was no difference in the smears, between follicular adenoma & follicular carcinoma. Only 4 cases out of follicular neoplasm/Hyperplastic colloid nodules with degenerative changes had histopathology available for comparison & revealed follicular neoplasm in 3 cases & colloid nodule in 1 case. All 18 cases of Hurthle cell neoplasm had histopathology which revealed Hurthle cell adenoma in 15 cases & Hurthle carcinoma in 3 cases. All the 9 cases of follicular carcinoma had histology available for comparison & confirmed the FNA diagnosis.2 of these had bone metastasis(Fig.3)

TABLE VIII
FNAC ---Thyroid (Neoplastic)
PAPILLARY CARCINOMA

FNAC Diag.	No.of cases	Age-years	Sex F/M	Hist.Diag.	No. of cases
1.Papillary carcinoma	135	8-80	113/22	a)Papillary carcinoma	134
				b)Follicular adenoma	01
2.Follicular neoplasm	04	25-47	4/0	a)Papillary carcinoma	02
				b)Follicular-Papillary Carcinoma	02
3.Hurthle cell neoplasm	01	40	1/0	Papillary carcinoma with Hurthle cell metaplasia	01
4.Benign vascular neoplasm	01	38	1/0	Cystic Papillary carcinoma	01
		TOTAL			141

TABLE IX
FNAC—Thyroid (Neoplastic)
MEDULLARY CARCINOMA

FNAC Diag.	No.of cases	Age-years	Sex F/M	Hist.Diag.	No. of cases
1. Medullary carcinoma	11	17-55	7/6	Medullary carcinoma	11
2.Anaplastic carcinoma	01			Undifferen-carcinoma	01
3.Follicular neoplasm	01			Undifferentiated carcinoma	01

2. & 3. were immunoreactive with Calcitonin,CK &CEA.

TABLE X
FNAC—Thyroid (Neoplastic)
UNDIFFERENTIATED CARCINOMA

FNAC Diag.	No.of cases	Age-years	Sex F/M	Hist.Diag.	No. of cases
Undifferentiated carcinoma	12	35-65	9/3	Undifferent-carcinoma	12

TABLE XI
FNAC—Thyroid (Neoplastic)
non-HODGKIN'S LYMPHOMA

FNAC Diag.	No.of cases	Age-years	Sex F/M	Hist.Diag.	No. of cases
1.NHL-large cell	14	19-80	11/4	NHL-large cell	2
2. NHL-low grade	01			x	x

FNA smears of follicular neoplasm & follicular carcinoma can't be discriminated on cytology. However, some follicular neoplasms on a clinicopathologic basis can be categorized as follicular carcinoma.Cytologic criteria include large nuclei with irregular coarse chromatin. Some cytopathologists[12,16] claim to make a cytologic diagnosis of 75% of follicular carcinoma. Other limitations in the diagnosis of follicular lesions are seen in tumours with cystic degeneration, differentiation between hyperplastic colloid nodule & follicular neoplasm & pleomorphism seen in atypical nodules. In Hurthle cell neoplasm, apart from limitations of deciding between adenoma & carcinoma, other thyroid lesions with Hurthle cells must be considered in differential diagnosis. These include Hurthle cells in follicular neoplasm, papillary & medullary carcinoma, Hashimoto's thyroiditis & even hyperplastic colloid goitre.Papillary Hurthle cell carcinomas in particular need distinction from papillary carcinoma & papillary carcinoma with Hurthle cell metaplasia. Overall 70-90% of follicular neoplasms are detected by FNA & the proportion of carcinoma varies from 14-44%[5,32-33]. Hamburger et al[6] reported a false positive of 9.6% in a series of 501 follicular neoplasms. In this study there were 2 cases of false positive cases & cross diagnosis of papillary carcinoma for follicular adenoma/follicular neoplasm.

Papillary carcinoma

141 cases diagnosed on histopathology had preceding FNA available for comparison with a diagnosis of papillary carcinoma in 135 cases,follicular neoplasm in 4 cases,Hurthle cell neoplasm in 1 case & 1 case of hemangioma in anterior triangle of neck.There was no problem in the diagnosis of 134 cases including 110 cases of conventional papillary carcinoma including 9 cases of follicular variant of papillary carcinoma,4 cases of papillary carcinoma with Hurthle cell metaplasia & 12 cases of cystic papillary carcinoma with a sensitivity & specificity of 95%.However , there were 6 cases of misdiagnosis on FNA including 4 cases of follicular neoplasm which proved papillary carcinoma -follicular variant ; 1 case of Hurthle cell neoplasm which proved Hurthle cell variant of papillary carcinoma & 1 case of hemangioma in lateral neck which proved cystic papillary carcinoma on histopathology. The last case was misdiagnosed due to negligence because the hemorrhagic fluid was neither centrifuged nor subjected to clot processing.1 case of suggestive (suspected) papillary carcinoma on the basis of intranuclear vacuolations proved follicular adenoma.A similar case is reported in literature[31].

In conventional papillary carcinoma an accuracy of 94%[34] & 95%[35] have been reported.In one study of 8 cases of follicular variant of papillary carcinoma, the nuclear grooves ,observed in 100% was the most dependable parameter to differentiate from follicular neoplasm. Cystic papillary carcinoma thyroid have been posing problems for cytopathologists & over 40% of such tumours are missed on FNA[36]. In this study 12 out of 13 tumours were correctly diagnosed. 8 of tumours aspirated earlier at different centres had been diagnosed as colloid goitre and hemangioma.

Medullary carcinoma

11 out of 13 tumours in histopathology were correctly diagnosed on preceding FNA as medullary carcinoma ,1 case as anaplastic carcinoma & 1 case as follicular adenoma.The last 2 cases even on histopathology were undifferentiated•tumours & required immunohisto chemistry for confirmation & tumour cells were reative with calcitonin, CK & CEA.The diagnosis of conventional medullary carcinoma should not pose any problem to cytopathologists.The undifferentiated & variants need careful attention & immunohistochemistry for confirmation . Cytology of the typical & atypical tumours is well described in the literature.[25-26].

Undifferentiated carcinoma

12 cases of undifferentiated carcinoma diagnosed on FNA had confirmation by histopathology. Subsequently 2 of these were seen complicating large standing colloid goitres. The representative smear pattern of the tumours were highly characteristic with pleomorphic tumour cells, small cells, spindle cells & giant cells in various combinations.The background shows cell debris. Cytology of this tumour has been well described[28]. In experienced hands there is little to offer in differential diagnosis. In difficult cases immunoreactivity with thyroglobulin, CK will help to arrive at diagnosis.

Lymphoma

15 cases of Primary non-Hodgkin's lymphomas were diagnosed on FNA,14 of large cell type & 1 of low grade-MALT type.Criteria applied for diagnosis were same as in lymph nodes[29]. Incisional biopsy was available only in 2 cases which conformed to FNAC diagnosed of NHL-large cell.1 of these required immunohistochemistry for confirmation. Primary NHL thyroid are uncommon & most are of B-cell lineage with large cell lymphomas more frequent

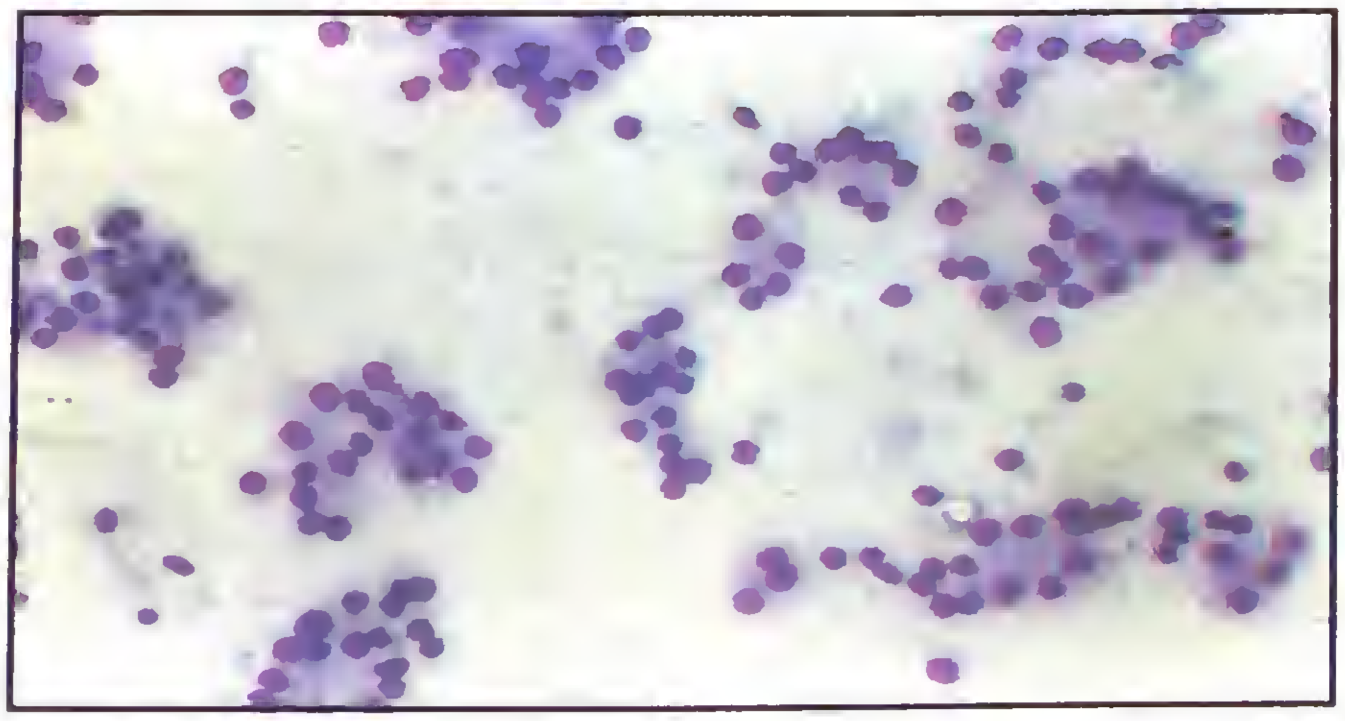

Fig.1.FNAC Thyroid-Follicular neoplasm shows follicular cells in micro-acini & some individually scattered cells. MGGx200

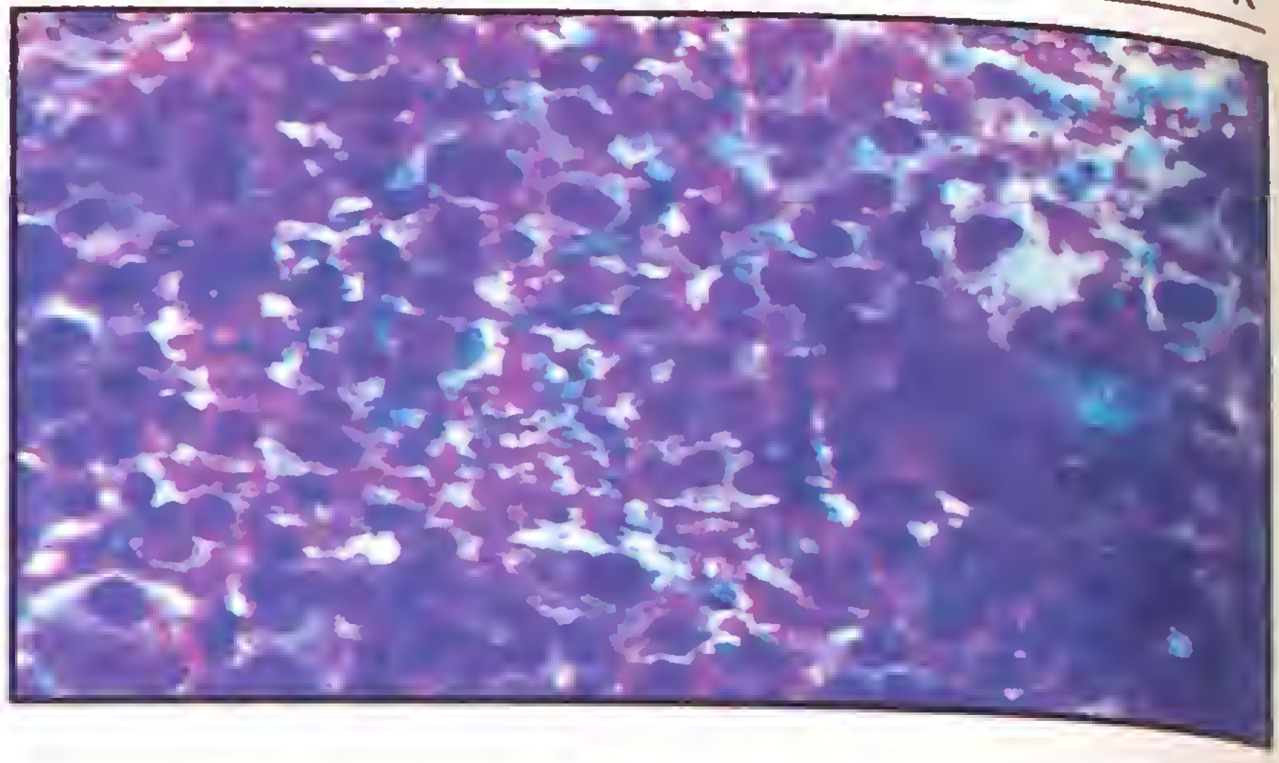

Fig 2.FNAC Thyroid -Follicular carcinoma shows follicular cells loosely arranged .Tumour cells larger than normal cells with large nuclei, coarse chromatin & prominent nucleoli in some cells. MGGx400.

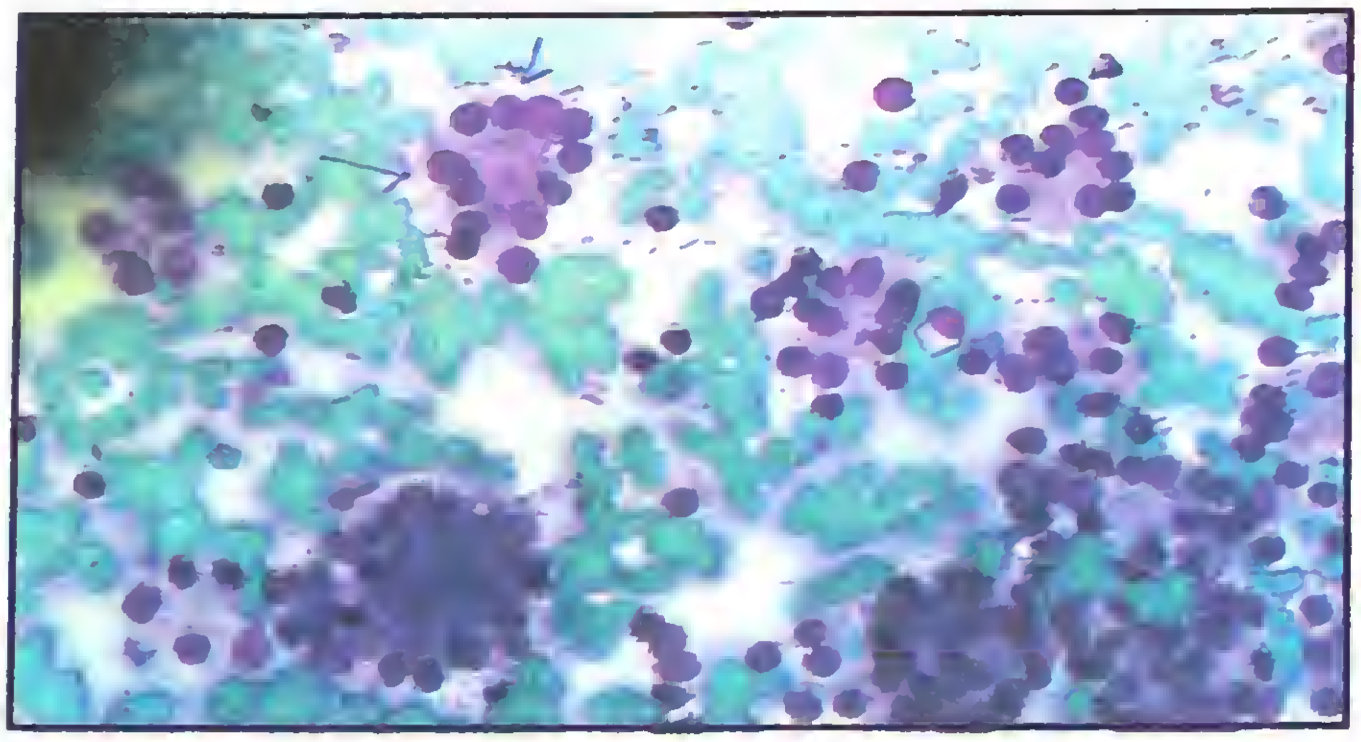

Fig.3. FNAC Pubic ramus-Metastatic follicular carcinoma,well differentiated ,with micro-acini arrangement.Colloid seen in lumen of an occasional acinus(arrow).MGGx400.

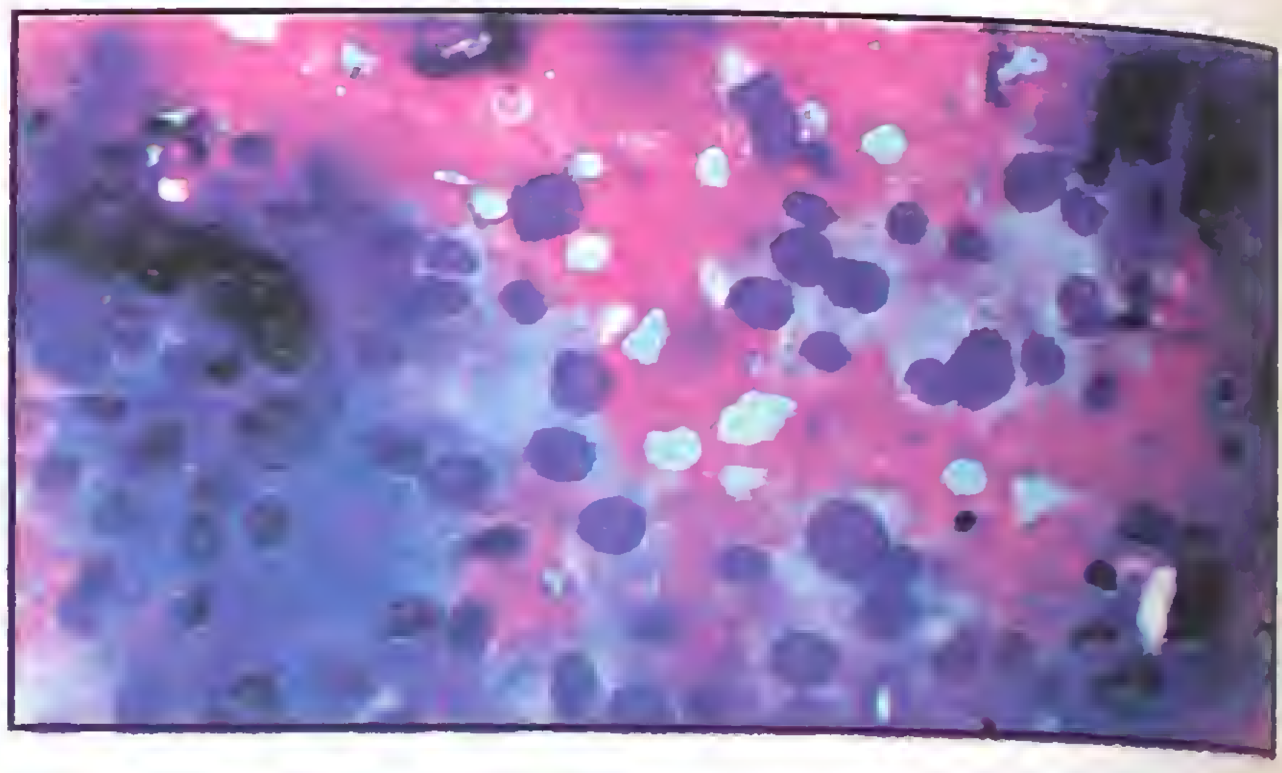

Fig.4. FNAC Thyroid-Hurthle cell neoplasm shows clusters of poorly differentiated Hurthle cells with abundant cytoplasm & large nuclei 1-2 with moderate anisonucleosis.MGGx400.

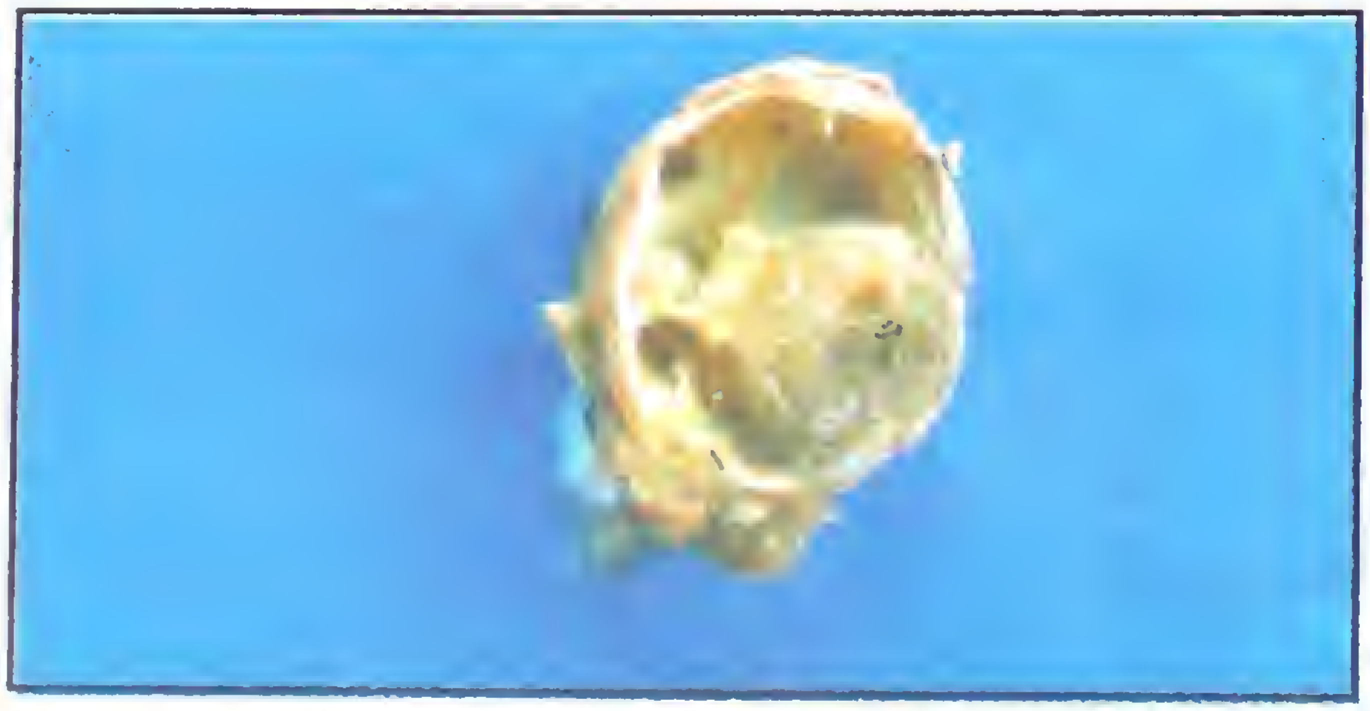

Fig.5 Gross specimen of follicular adenoma.A well capsulated tumour ,solid & cystic.These smears may be hard to interpret & may be labelled Follicular Neoplasm\Hyperplastic Nodule with degenerative changes.

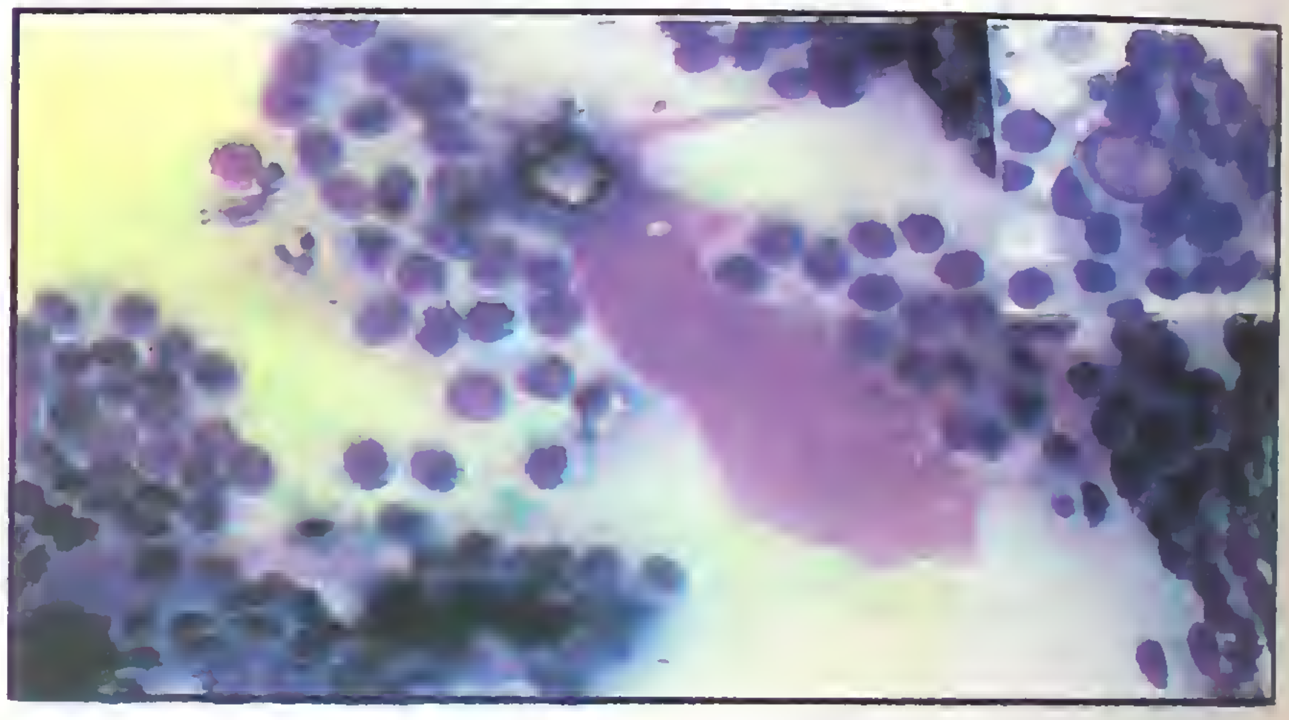

Fig.6.FNAC Thyroid-Papillary carcinoma shows typical tumour cells in monolayered sheets & papillae & thick ropy colloid.Inset-right upper corner ,a cell with large intra-nuclear vacuolations.MGGx400.

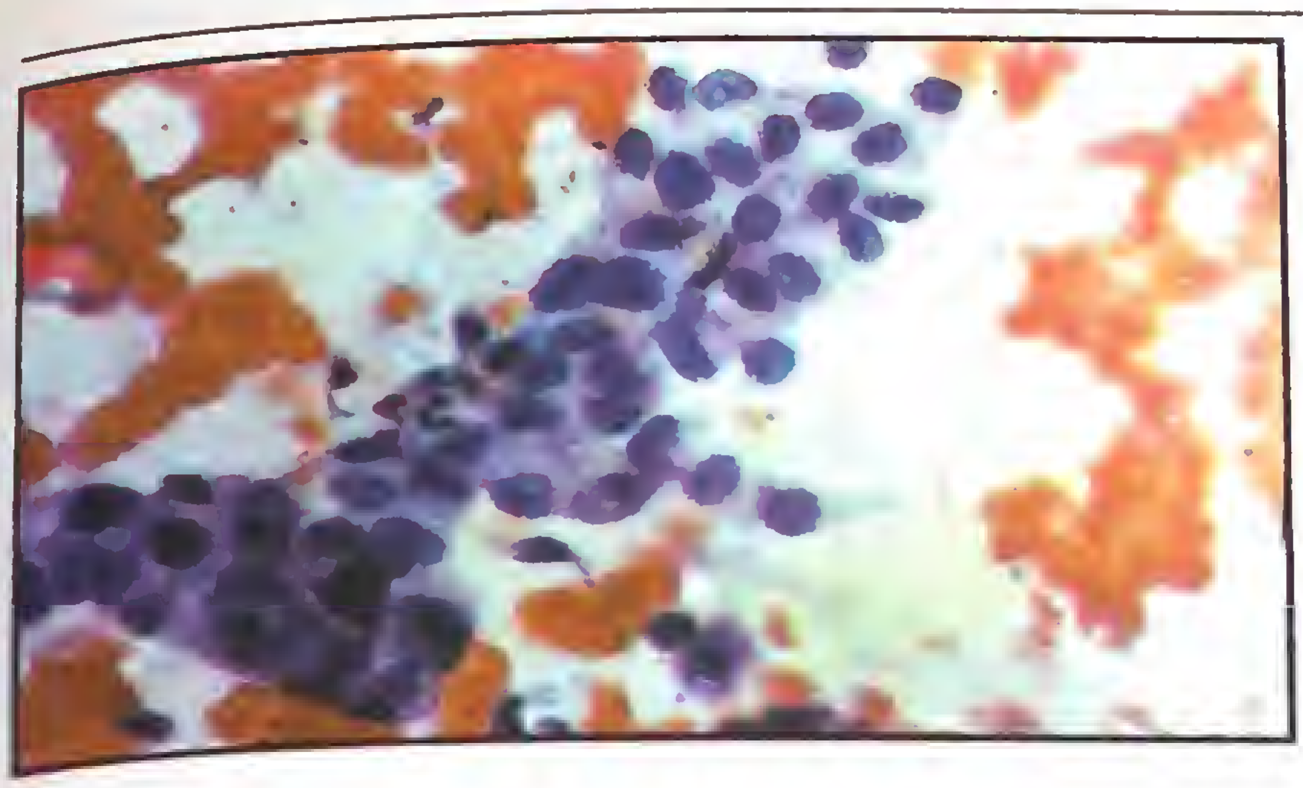

Fig.7.FNAC Thyroid- Papillary carcinoma.Tumour papillae with nuclear grooves.H&Ex400.

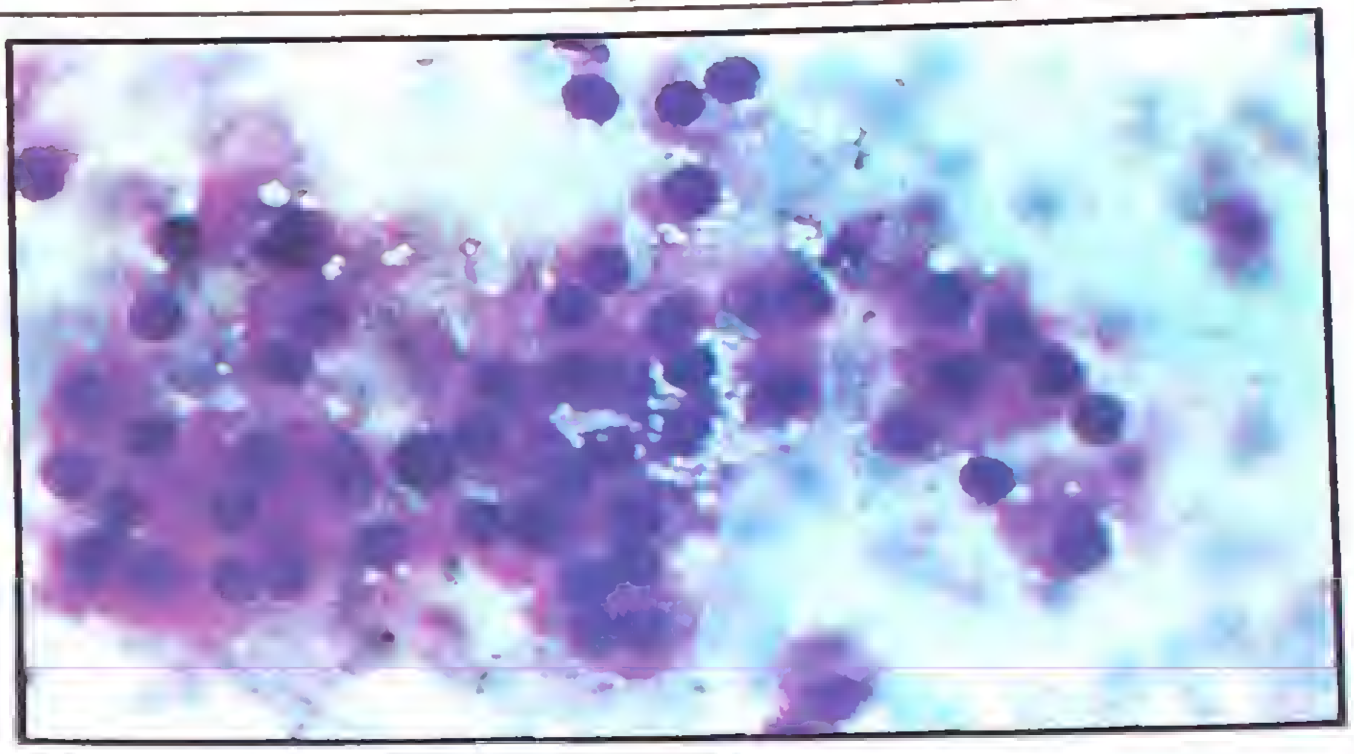

Fig.8.FNAC Thyroid- Papillary carcinoma-Follicular variant often interpreted as follicular neoplasia as in this case.Shows tumour cells in poorly formed follicles.Nuclear chromatin may help to arrive at correct diagnosis.MGGx400.

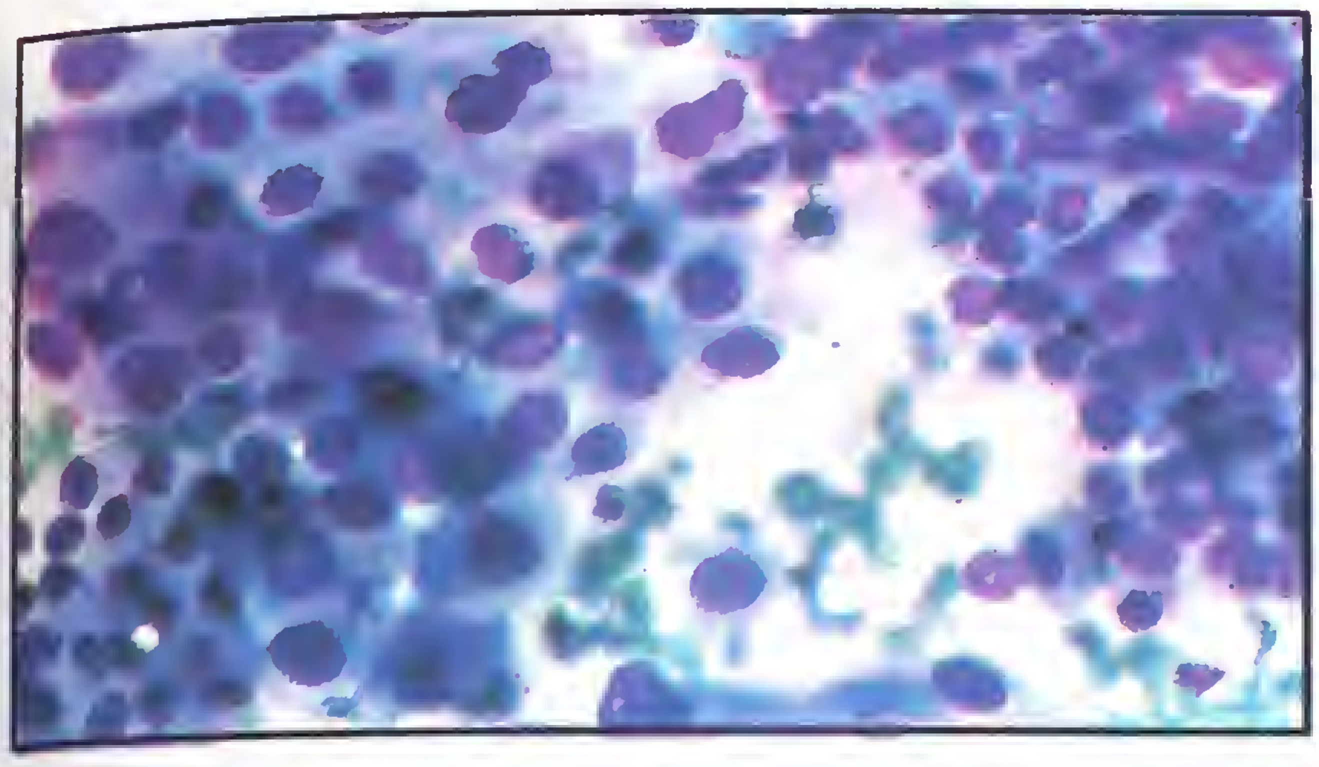

Fig.9.FNAC Thyroid-Papillary carcinoma wiyh Hurthle cell metaplasia .Hurthle cell occupying left hand of the field with occasional intranuclear vacuolations.MGGx400.

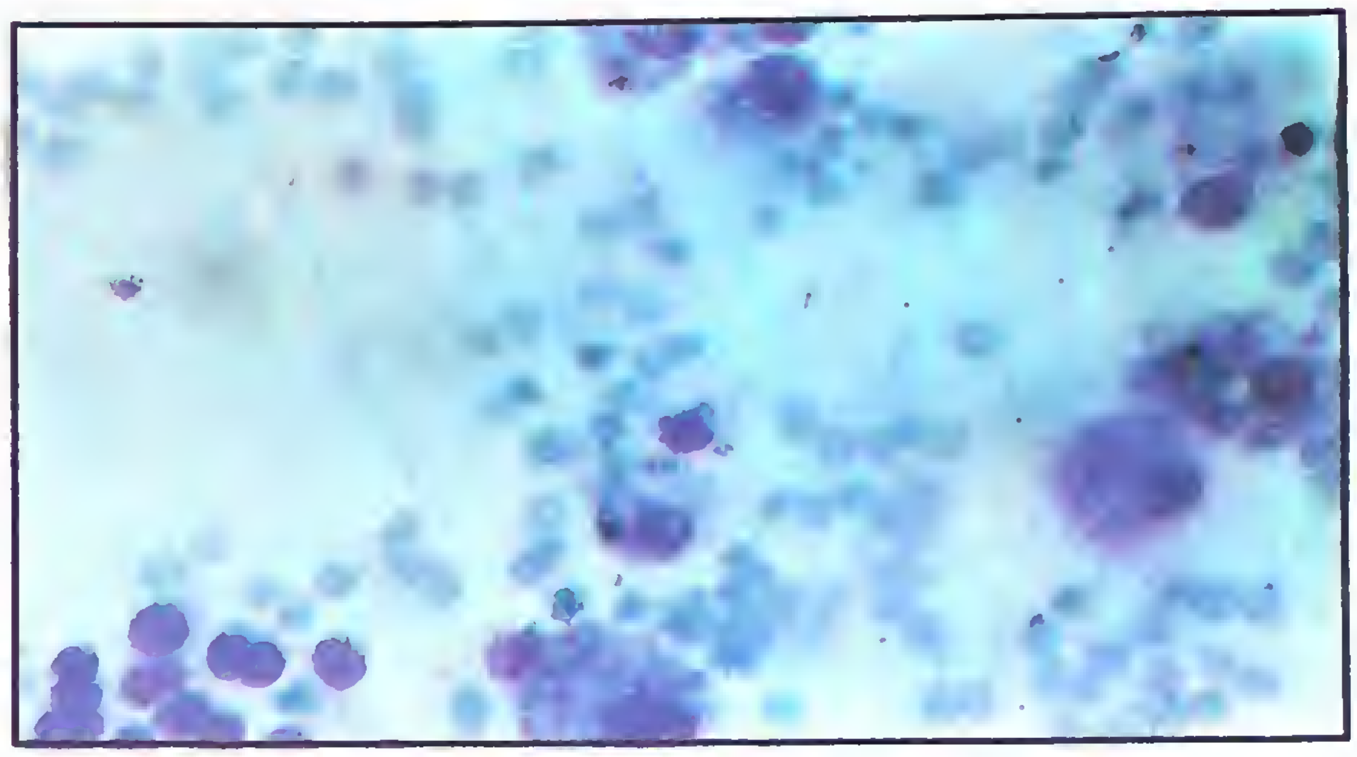

Fig.10.FNAC Thyroid .Papillary carcinoma-Cystic.Tumour cells with vacuolated abundant cytoplasm mimicking macrophages .Typical carcinoma in one corner.MGGx400.

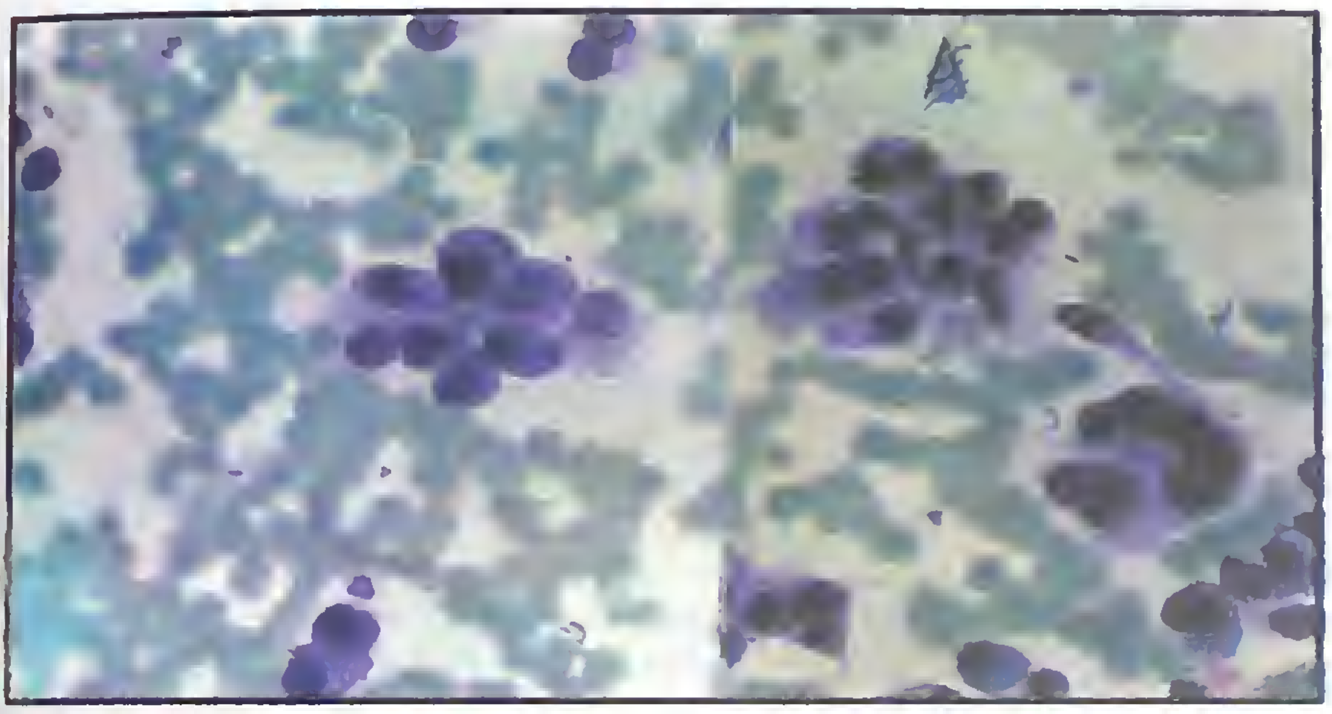

Fig.11.FNAC Thyroid - Medullary carcinoma shows typical, plasmacytoid tumour cells dispersed & loose clusters. A tumour giant cell with multiple nuclei. MGGx400.

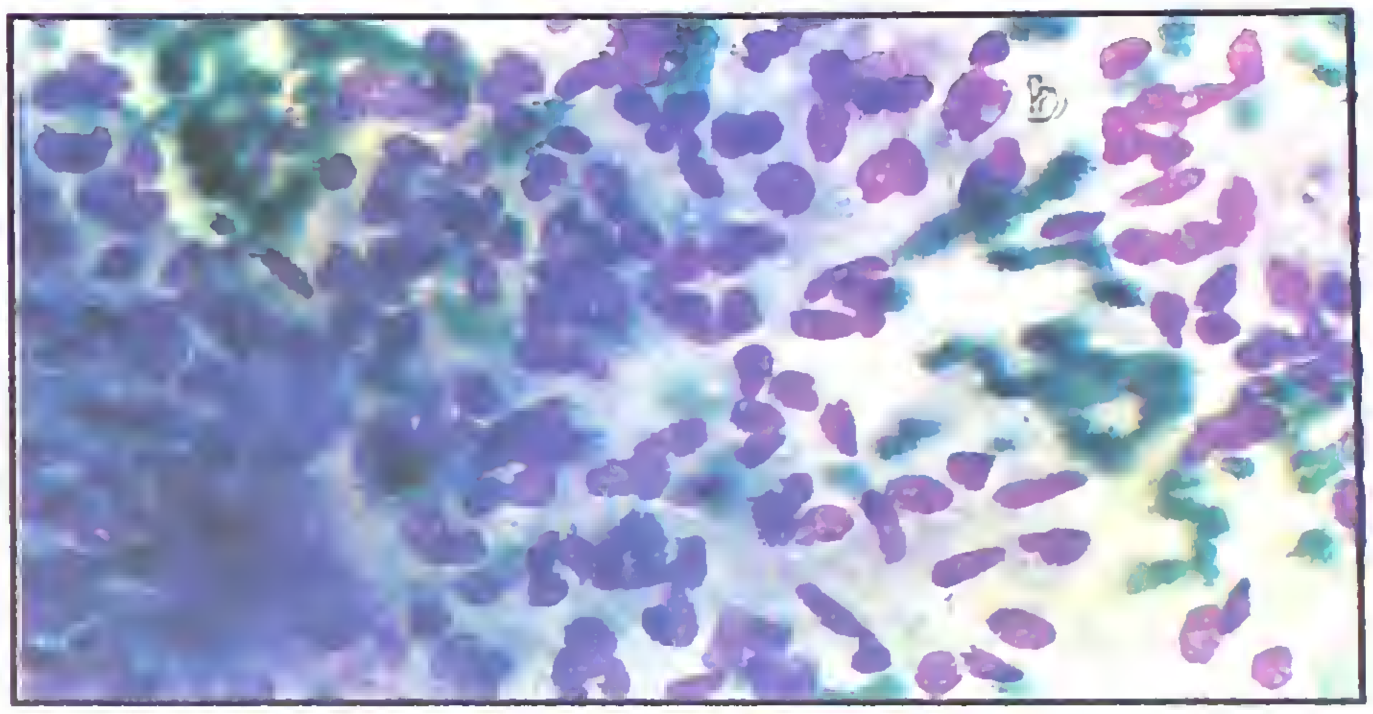

Fig.12.FNAC Thyroid - Medullary carcinoma of spindle cell morphology. MGGx400.

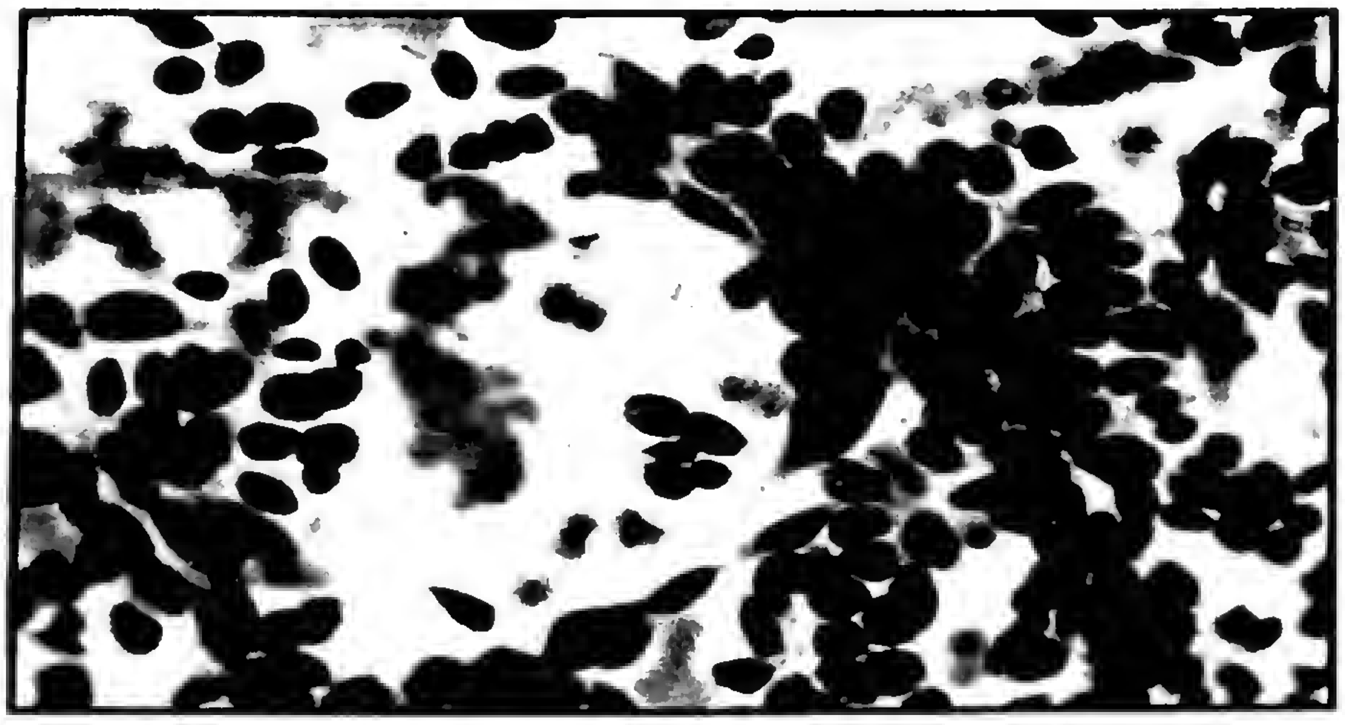

Fig.13.FNAC Thyroid-Medullary carcinoma of small cell type. Undifferentiated. Required immunohistochemistry for confirmation. MGGx400.

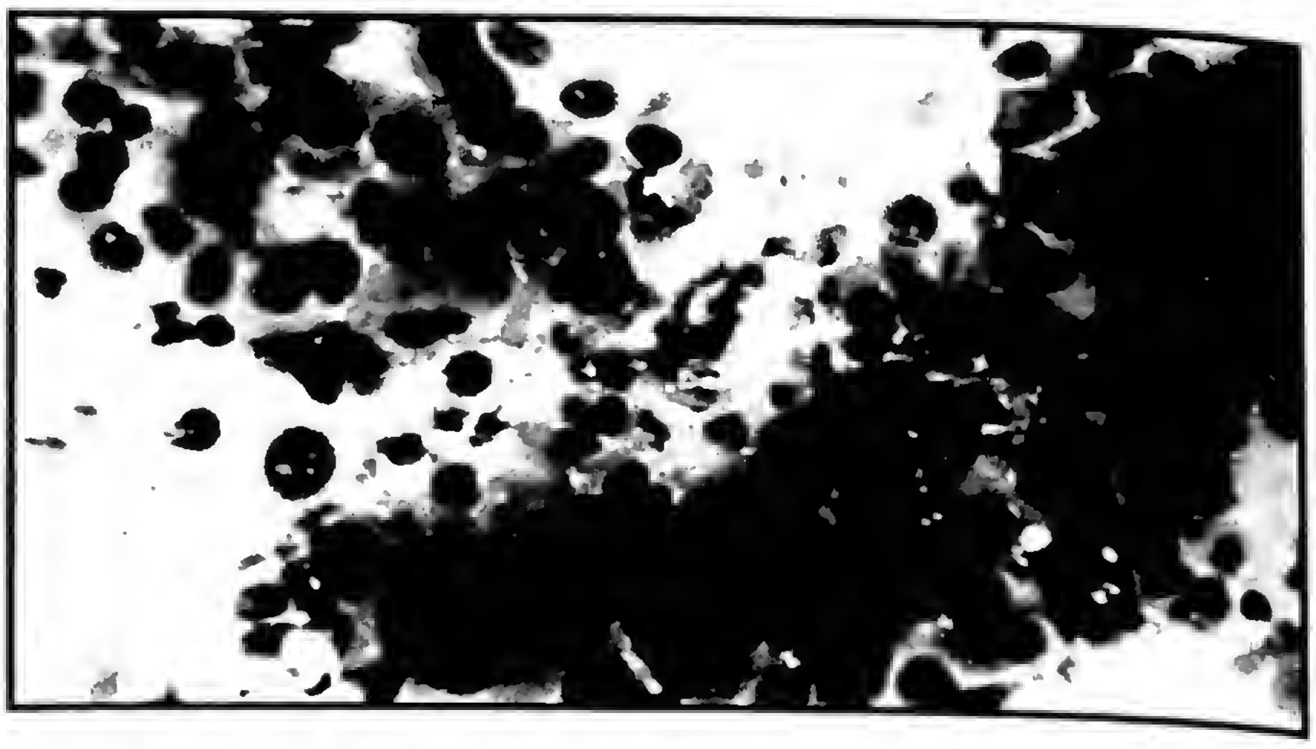

Fig.14.FNAC Thyroid-Undifferentiated carcinoma shows tumour cells with considerable variation in size & shape including tumour giant cell.

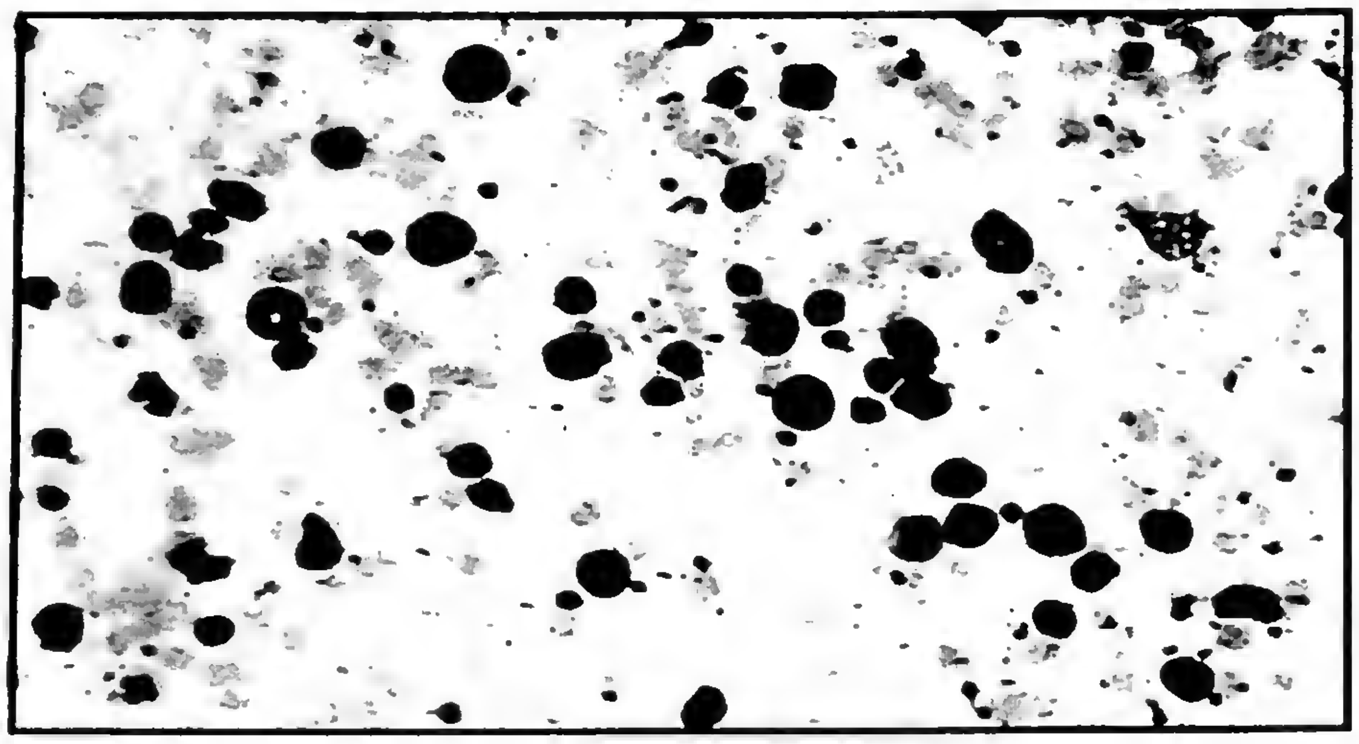

Fig.15.FNAC Thyroid-NHL -large cell-shows dispersed large lymphoid population with lympho - glandular bodies. MGGx400.

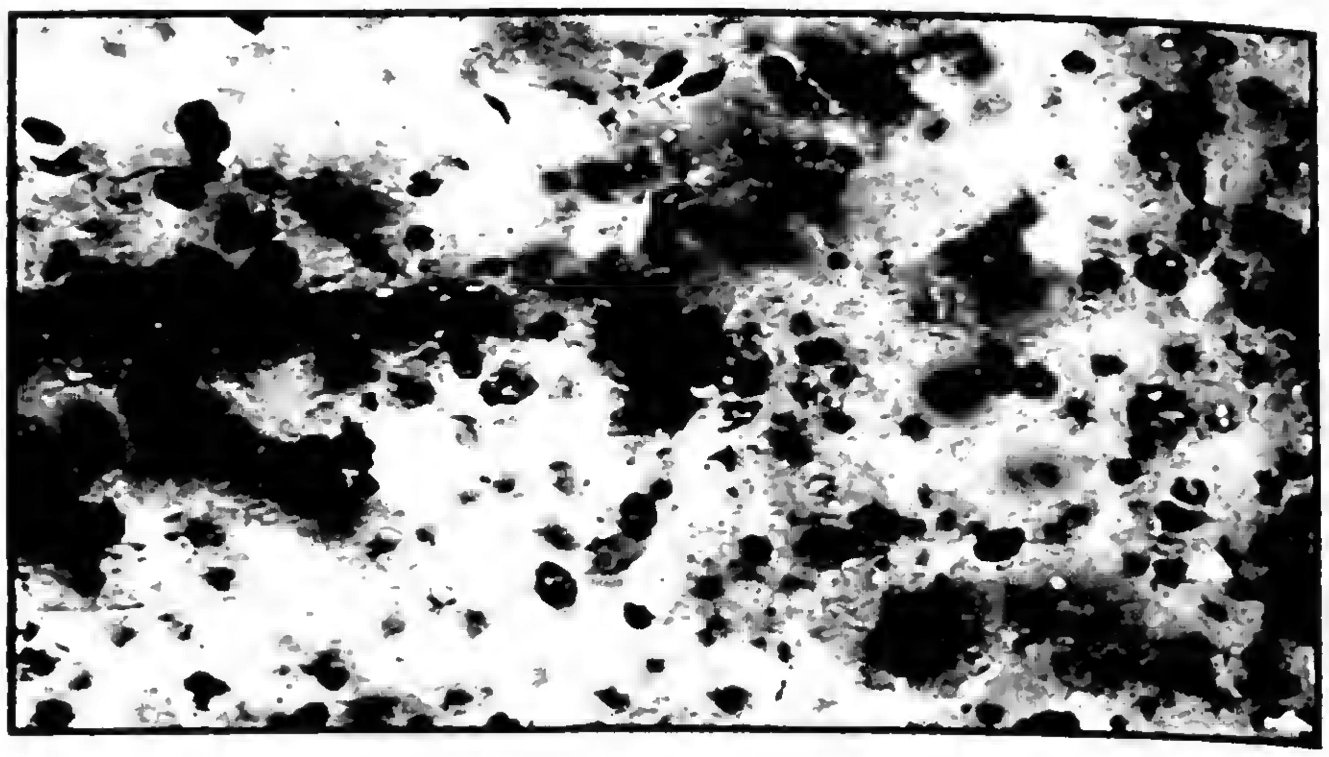

Fig.16.FNAC Thyroid-Metastatic squamous cell carcinoma from larynx shows moderately differentiated squamous cancer cells with necrotic debris.MGGx400.

than low grade MALT lymphomas.[37] The majority are reported to be associated with Hashimoto's thyroiditis[38]. Lymphomas diagnosed on FNAC are rarely reported in literature[30,39-40].

Metastatic malignancies

The thyroid is a relatively common site for metastatis in disseminated malignancy .Lung ,gastrointestinal tract, breast, kidney,melanoma and lymphoid tumours are the most common to metastasize to thyroid.[41-42]. In patients of known malignancy ,diagnosis may not be difficult ,otherwise renal cell carcinoma ,anaplastic small cell carcinoma & spindle cell melanoma can simulate primary tumours like follicular, insular & medullary cancers. The authors have reported 9 cases of metastatic cancers to thyroid. 8 of squamous morphology & 1 of adenocarcinoma. The primary sites were esophagus & larynx.

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INSTALLATION,COMMISIONING AND QUALITY ASSURANCE OF COBALT UNIT (THERATRON 780E) AT SKIMS,SOURA,SRINAGAR

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ABSTRACT

The Sher-i-Kashmir Institute of Medical Sciences,Soura,Srinagar started functioning in June, 1982. However, the department of Radiation Oncology started treating cancer patients in 1984 with the commissioning of Co-60 (Theratron -780), teletherapy machine, first of its kind in the state with a source strength of 10734 ci. Another Teletherapy machine Mevetron-74 (Linear Accelerator) was also commissioned in the same year.The accelerator started malfunctioning, resulting an extra load of patients on Theratron-780. Consquently, the patients planned for therapy by linear accelerator used to be shifted to cobalt machine for treatment. This put a heavy load of patients on cobalt and consumed many working hours of Dosimetrists. The linear accelerator went out of function permanently in 1990. Obviously, all the work load of the patients had to be put on Theratron-780. Keeping in view the possible and sudden breakdown of Theratron-780 due to heavy patient load and delay in treatment to cancer patients, department of Radiotherapy procured another cobalt 60 unit Theratron 780E a better version of Theratron 780 with a source strength of 10,684 ci.

It is mandatory to conduct quality assurance and commissioning tests of ionizing radiation emitting equipments. The competent agency to do so is Bhaba atomic Research Centre, Mumbai. Since the Department of Medical physics & Bio-Engineering is equiped with most modern tools for conducting such tests, therefore,BARC authorized the Pysicists and Radiation Safety Officer of this Institute to conduct such tests. Discussed in this paper are the quality assurance and commissioning tests of THERATRON-780E, the tests are found in coherence with ICRP &ICRU regulations.

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INTRODUCTION

Radiation was probably used in Cancer treatment before it was employed in diagnosis. High energy photons and electron beams are now widely used in radiation therapy.In India, for treating cancer by external Radiotherapy, majority treatment plans are carried by Cobalt 60 gamma radiation.

The role of physicist in radiotherapy is to convert a qualitative medical intention into a precise quantitative course of action. The radiotherapist prescribes the treatment, the physicist translates the prescription into a practice by delivering the required radiation dose to the designated target volume, without over dosing normal tissues outside that volume.

The Physicists traditional domain is the teletherapy machine, Cobalt unit in the present case. In recent years, however physicists sphere of interest has enlarged to include the localization of the tumour and the assessment of patients anatomy (through imaging and other techniques) and the problems arising during the actual setting up of subsequent irradiation of the patient.Besides this the quality assurance of the equipment used for treatment and the tools used for calibration and maintenance of equipment are included in this job. In India Cobalt teletherapy machines are predominantly used for radiotherapy.

Cobalt-60 is a radionuclide produced in a nuclear reactor by activating 59Co with neutrons. Cobalt-60 is primarily a beta emitter(maximum ß-Energy 0.31 Mev) which decays into an excited state of 60 Ni with a half life of 5.27 years. The excited nucleus of 60 Ni gives up its excess energy by emitting two gamma photons cascade, with energies of 1.17 and 1.33 Mev,the median energy being 1.25 Mev. The radiation from a Cobalt unit is usually considered to be monoenergetic(1.25 Mev). As a first approximation this is certainly true. However, the photon spectrum is in practice quite complex, since it includes secondary scattered.(Compton)Photons from the source itself, from the source capsule, its housing, and from the collimator.In addition there is a modest amount of low-energy brehmstrahlung produced when the betas are absorbed in the source capsule.

The first cobalt unit (Theratron 780) was installed in the department of Radiotherapy at SKIMS in December 1983 with cobalt source of 10,734 curies. This had an output of 2.75 Gy/mt at 80 cms for 10cmx10cm field size. The strength of source and output dropped every year. The strength was 1935.94Ci and output was less than 0.50Gy/mt on the date when the source was changed by a fresh source.The new source was having strength of 10,684 ci on 22.11.95.Its output was 2.806 Gy/mt at 80 cms for 10x10cms field size on 26.12.96. The need for change of source is that i) once output falls below 40 Gy/mt, the time of irradiation increases which is not desirable for patients who have gone weak due to the disease with the result their mobility is difficult to control. ii) Cobalt unit has number of mechanical moments which gives rise to lot of wear and tear of the machine. Besides changing the source in the old machine the SKIMS acquired one more cobalt unit namely Theratron-780 E a better version of the previous machine.

Before a therapy unit could be used for treating patients, number of physical measurements need to be performed. After these initial measurements have been made, periodic checking of different items are necessary to ensure accurate delivery of radiation. This programme is commonly known as quality-assurance of the equipment. The programme is accepted world wide and can be seen in various IAEA,ICRU,ICRP,ANCI & AERB rules and reports.It implies a programme of tests,checks or procedures designed to ensure an end-product of consistently high quality. In radiotherapy as stated earlier also, the end product is the treatment of the patient by ionizing radiation and quality assurance procedures are needed to ensure that the prescribed radiation dose is, in fact, delivered to the target volume in the patient with as little error as possible preferably an error of less than1 ± 5%. Special procedures are required to maintain a Cobalt-60 unit in good working order and ensure that the mechanical moments, optical and radiation system operate within the specified tolerance limits. The accepted world wide limits for each are prescribed in Atomic Energy Regulatory Board,IAEA,ICRU,ANCI ,ICRP rules & regulations.

The physics quality assurance section is divided into 1) Dosimetry 2) treatment planning 3) radiation machines 4) simulators 5) radiation safety. Each of these section involve number of separate checks needed to ensure the accuracy and safety of treatment.

Discussed in this paper are the installation, commissioning, quality assurance & Radiation safety of Theratron 780E Cobalt machine installed in department of radiotherapy SKIMS.

MATERIAL & EQUIPMENT

Cobalt therapy unit under the trade name 780-E was supplied by M/s MDS Nordian, Canada INC. This equipment was commissioned on 1.7.2001. The source strength was 354.5 TBq (9580ci) on Jan 12, 2001 Farmer type dosimeter of Nuclear Enterprises, U.K was used to find the exposure and dose. An ion chamber 2571 was used for dosimetry.Pocket dosimeter & Gun monitor was employed for radiation safety. RFA from M/S Therados, Sweden was used for checking congruence between optical & Radiation fields. Wisconison tool kit for RT was used to check the accuracy of other parameters of the unit.

METHODS & RESULTS

Once the equipment was installed the tests for commissioning were performed.

a) Mechanical & Collimeter

The equipment passed the mechanical tests including the motions of the collimeter.

b) Shift in optical field due to vertical motion from minimum to maximum position:-

A field size 10cmx10cm was drawn on a paper & centre of field was marked. The paper was placed on treatment table and centre brought at 80cms SSD. The optical field was coincided with the drawn field along the centre. The table was brought to first minimum position and then to maximum position. A shift was observed during this travel. This was corrected to 2.0 mm which is within tolerance limits (=2m)

c) Shift in optical field due to rotational motion from -90 to + 90.

With the above drawn field & centre coinciding the gantry was rotated from -90 to +90. Again a shift was observed. This was corrected to 1.00 mm which was also within tolerance limits (= 2mm).

d) Optical beam & collimeter arms coincidence.

In the above experiment the collimeter was rotated & the shift in coincidence was corrected to 0.5mm which is within tolerance limts
(= 1mm).

e) Optical field overlap

The optical field was marked at a position when Gantry was on 00 positions. The gantry was then rotated through 180o. The overlap was observed which was less than 1 mm (tolerance = 1mm).

f) Iso- centre

A thin needle with sharp point was placed on table. The tip was adjusted at 80 cms from the source. A graph paper was placed on beam shield. The shadow of the tip was marked. This all was done on 00 degree. Gantry position. Gantry was then rotated through 1800. The shift in the position of pointer shadow from 00-3600 was observed. This was adjusted to < 1mm whereas tolerance is = 4 mm.

g) The other tests like rotational angle, parallelism of jaws orthogonality of jaws, symmetry of jaws, Head Swival etc were found in agreement with the prescribed tolerance limits.

h) Read-out Accuracy SSD or SAD verification.

Table 1) refers to the stated and measured values for mechanical front pointer, optical distance indicator and laser beam indicator. No discrepancy was found.

i)Field size(Fs) definition

Field size is defined as the opening of (x, y) jaws measured at treatment distance (80cms). Table (2) refers to the stated and corrected field size. They have been set within the tolerance limits.

j) Optical distance indicator (ODI) scale verification:

All ODI readings from normal treatment distance to ± 20 cms are within tolerance of ± 1.5 mm

RADIATION CHECKS

Congruence between optical and Radiation fields.

A paper packed therapy verification film with build up of 5mm is placed at treatment distance. The optical field is set at 10cms x 10 cms on the film surface. Angled lead wires were placed on the corners of the optical field and also on the lines define the cross-wires (but outside the field). The film was exposed to 20 R to get an optical density of nearly one. The densities were masured using the following instrument:

i. Densitometer
ii. Radiation field analyzer (AB Therados)
iii. RFA(Scandi tronix)

The exposed films and density patterns are shown in fig (1a, 1b). Radiation field has been measured in 50% width in two orthogonal directions given as

L to R : 10.2 cms
G to F : 10.2 cms

This is within tolerance limts = 2mm

Output calibration

Before the equipment is used for the treatment purposes its following parameters are estimated and compared with those supplied by manufacturer. The equipment is used for treatment once these parameters are within the limits prescribed by various protocols.

1.Shutter timer error:

It is important to determine the relationship between exposure time and set time on the timer. The difference arises from "end errors" at the beginning and at the end of exposures. At the beginning of exposure, the exposure rate rises from zero to its steady value over a finite period of time. Similarly at the end of exposure, the exposure rate does not necessarily fall to zero instantaneously and these end errors give rise to what we call "Timer error" (Table 3)

Shutter timer error was evaluated by double exposure technique.

The centre of the thimble chamber (with build up cap) of Farmer dosimeter was placed at the normal treatment distance. Five exposures, each of time t were given and calculated the average reading R1. Next two consecutive exposures of (t/2 +t/2) were also given. Calculated the average of five such readings as (R2). Computed the shutter timer error as per the following equation:

$$\delta t = \frac{(R2-R1)\times t}{2R1-R2}$$

2.Output calibration for different field sizes

The output is different for different field sizes. Hence it is essential to find Normalized output factor(NOF). A calibrated chamber(with appropriate build-up cap) was placed at cenrtre at SSD + dm. in the present case is 5mm for Cobalt- 60. The room temperature and pressure at the start and after completion of the measurement was noted. The chamber position was adjusted so that it is exactly centered in the field size 10cmx10cm. At least 3 readings were taken and average values for the field size taken. The exposure time was set as 1.00 mins. The output is given by:

$$= R \times CF \times F_{tp}$$

where
R=metre reading
CF=chamber caliberation factor
F_{tp}= Pressure, temperature correction factor

Also, normalized output factor, NOF is defined as

$$NOF = \frac{\text{output for a given field size}}{\text{output for 10cmx10cm field size}}$$

The table: 4 shows the NOF w.r.t. different field sizes.

TABLE 1
Read-out Accuracy

SSD or SAD verification

	stated	Measured
Mechanical frontpointer	35 cm	35 cm
optical distance Indicator	60 cm	60 cm
Laser beam Indicator	-	0mm

Tolerance: <±1.5 mm

TABLE 2
Field size (Fs) definition

Set optical Field size cmxcm	Measured	Optical field	Size at Gant cmxcm	Position	Tolerance
Angle	0°	90°	180°	270°	for Fs<=
5x5	No error	No error	No error	5x5.1	10cmx10cm
10x10	-do-	-do-	-do-	10x10.1	<=1mm
15x15	-do-	-do-	-do-	15x15.1	for Fs>
25x25	-do-	-do-	-do-	25x25.1	10cmx10cm
30x30	30x29.95	-	-	30x30.1	<=2mm
35x35	No error	-	-	35x35.1	

TABLE 3
Shutter timer error

S. No.	1	2	3	4	5	Ave.	Timer error
R1	228.5	228.7	228.7	228.7	228.7	228.66	+0.02 min
R2	233.5	233.5	233.5	233.5	233.5	233.50	

3.Wedge factor

The isodose distribution for a given radiation field is often altered purposely with special absorbing device inserted into the beam to suit some special situation. The most commonly used device used in radiotherapy is the wedge filter. At the point of intersection of the isodose curve with the central axis of the field, the angle, between the isodoseline and the normal to the central axis is called the wedge angle, which is defined as the degree of elevation of the isodose curves from the horizontal. The use of wedge fields in treatment planning is numerous. The main goal is to achieve uniform dose in the tumour volume in cases where the use of normal fields is hard to achieve for one reason or the other.

The wedge filter, as an absorber, introduced in the field reduces the dose on the central axis by an attenuation factor defined as wedge factor (WF) where

WF = Exposure in presence of wedge filter (R2)
Exposure under identical conditions of irradiation in absence of the wedge filter (R1)

To determine WF, the chamber with appropriate build up cap was placed at SSD +0.5cms. The collimeter jaws were set to correspond to wedge field being used the average of five readings for the field give R1. Inserted the wedge filter in its holder and again average five readings were taken under identical conditions. This gives R2.

TABLE 4
Output factors

Field size cmxcm (1)	Meter reading for time t min a	b	c	ave	Corrected output SSD+ 0.5cm R/min (2)xCF	Normalized output factor (NOF) (4)
5x5	45.8	45.8	45.7	45.76	261.84	0.955
10x10	47.9	47.9	47.9	47.90	274.08	1.000
15x15	49.6	49.7	49.7	49.66	284.15	1.036
20x20	50.7	50.7	50.7	50.70	290.10	1.058
25x25	51.3	51.3	51.4	51.33	293.71	1.071
30x30	51.5	51.5	51.5	51.50	294.68	1.075
35x35	51.4	51.4	51.4	51.40	294.61	1.074

TABLE 5
Wedge transmission factors

S. No.	Wedge angle	Wedge field size	Measured value	Specified by the manufacturer
1.	30^0	6x15 cm^2	0.791	0.787
		8x15 cm^2	0.752	0.751
		10x15 cm^2	0.716	0.713
2.	45^0	6x15 cm^2	0.684	0.683
		8x15 cm^2	0.623	0.631
		10x15 cm^2	0.582	0.581
3.	60^0	6x15 cm^2	0.553	0.550
		8.15 cm^2	0.479	0.471
		10x16 cm^2	0.415	0.409
4.	15^0	15x20 cm^2	0.684	0.678

TABLE 6
Renewable depth dose data

Depth	Calculated values	Stated values	Difference
0.5cm	100.00	100.00	00.00
1.0 cm	98.32	98.20	00.12
2.0cm	93.92	93.30	00.62
3 cm	87.62	88.30	00.68
4 cm	83.93	83.40	00.53
5 cm	78.65	78.50	00.15
6 cm	78.65	73.60	00.04
7 cm	67.88	68.80	00.92
8 cm	64.32	64.10	00.22
9 cm	59.64	59.70	00.04
10 cm	54.85	55.60	00.75

Table. 5, shows the measured wedge factor and specified by manufacturer. We always use the measured values for treatment purposes.

TABLE 7
Tar Data

Depth	Calculated values	Stated values	Difference
0.5cm	1.034	1.036	0.002
1.0 cm	1.026	1.028	0.002
2.0cm	1.007	1.002	0.005
3 cm	0.969	0.971	0.002
4 cm	0.939	0.938	0.001
5 cm	0.904	0.902	0.002
6 cm	0.863	0.864	0.001
7 cm	0.829	0.825	0.004
8 cm	0.784	0.785	0.001
9 cm	0.748	0.746	0.002
10 cm	0.704	0.707	0.003

TABLE 8

Measurement Position	exposure rate 1	2	3	4	5	Average
Primary Barier1	<1MR/h	<1MR/h	<1MR/h	<1MR/h	<1MR/h	<1MR/h
Primary Barier 2	-do-	-do-	-do-	-do-	-do-	-do-
Above ceiling	Not accessible					
Below floor	No occupancy					

4. Percentage depth dose

Since there is a point where the absorbed dose is maximum(maximum abs.dose) within a phantom, the dose at any other point with reference to maximum dose is expressed as % of the maximum dose,the data is independent of source strength , however dependent on field size.

% DD at a point = Dose at this point x 100
Dose at maximum dose point

In full scatter water phantom,an ion chamber was placed in the slot provided. The water level was adjusted to SSD 80 cms. The ion chamber was connected to Farmer dosimeter. The desired field size was opened. Dose at different depths were taken including at depths of maximum dose (0.5 cm present case). %DD was calculated in accordance with the above formulae. The Table:6 represents the % DD according to the depth.

5.Tissue Air Ratio) TAR

Tissue Air ratio (TAR) is used to calculate the absorbed dose on the central ray of radiation beam.

TAR = Abs. dose in a phantom with d cm of over lying tissue
Abs. dose at the same point with just enough phantom build up material

Table (7) shows the actual TAR for different field sizes for the machine under test.

RADIATION PROTECTION SURVEY

As in all modes of radiotherapy radiation protection in cobalt-60 therapy involves protection of the patient, technical staff.

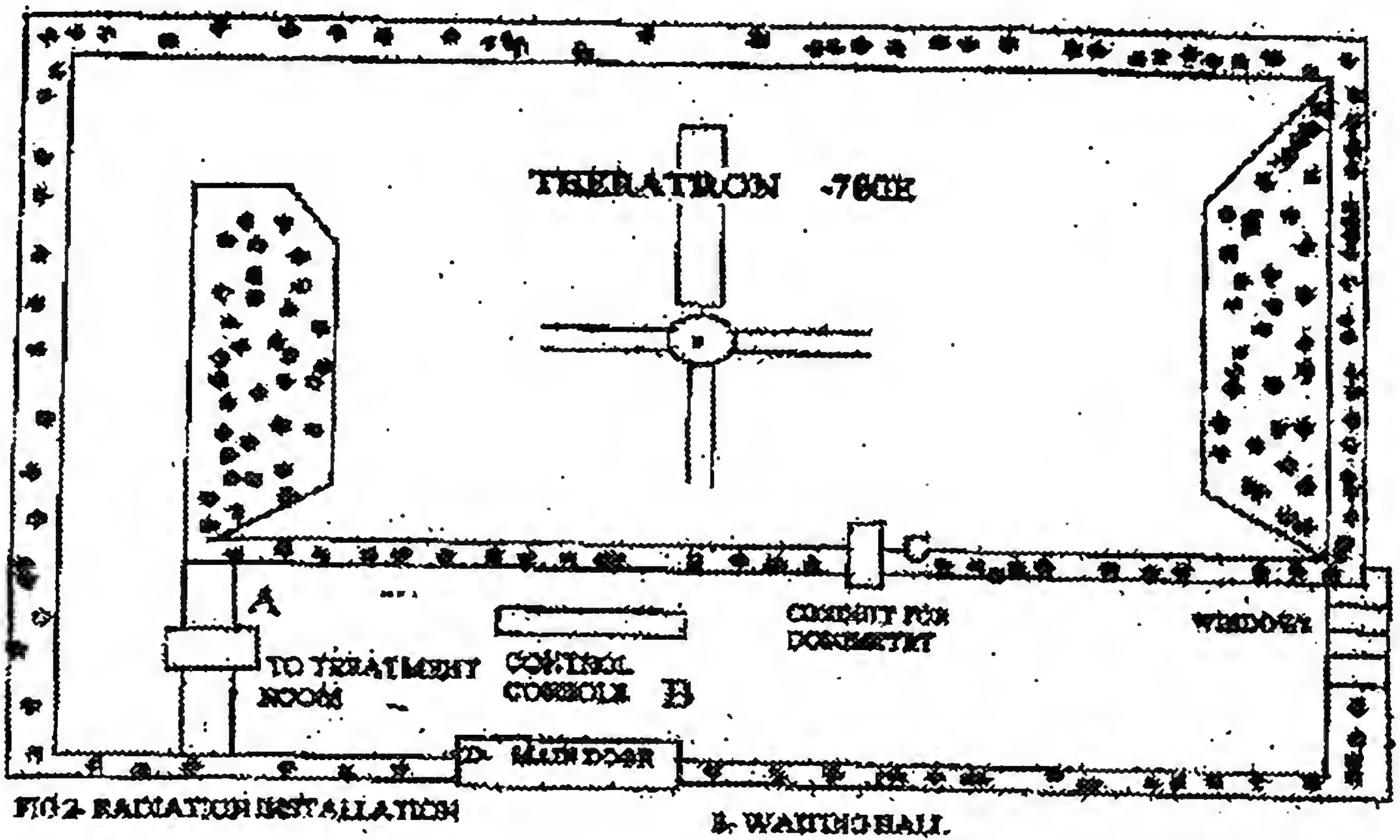

FIG 2- RADIATION INSTALLATION B- WAITING HALL.

hospital personal and the public at large. Safety is dependent on equipment design and construction, staff training, working procedures (including dosimetry) and the application of appropriate safety rules. From the point of view of the patient, the design of cobalt unit and the effectiveness of dosimetry, setting up and other procedures are all important. For radiotherapy staff involved in execution of treatment both equipment design and room design are important. For everyone else, protection signified isolation of radiation from the surroundings by means of room shielding.

Radiation leakage in the machine

a) Head leakage:

source off condition

Measured exposure rate (mR/h)	Measured positions							
At 5 cm from the surface	1.	2.	3.	4.	5.	6.	7.	8.
of the Source head.	6.44	8.28	3.68	3.68	1.84	1.69	1.84	0.92

Tolerance: ≤ 20mR/h when unit is loaded with maximum capacity source

b) Measured exposure rate (mR/h) at 1 m from the source= 0.92

Tolerance: ≤ 1 mR/h when unit is loaded with maximum capacity source.

Source 'ON' condition

Measured exposure rate at 1m from the source with collimeter jaws completely blocked with appropriate lead thickness.

Maximum 7.038R/mt

Minimum 0.879R/mt

Tolerance ≤ 0.1 % of RMM of the loaded source.

Collimeter transmission

The collimeter transmission is measured over a range of field sizes at a distance of 1 meter from the source. The collimeter transmission measurement points were chosen outside of useful beam opening, but not beyond the maximum definable field size = 3.55 R/mt

Tolerance : 2% of RMM of the loaded source.

Couch transmission

This test was performed by using farmer dosimeter at the entrance point of treatment table and at the exit point of treatment table, the observations were found within the tolerance limits.

SURVEYS

a) Ref to the Fig: 1 of the radiation installation.

The areas occupied by radiation and non radiation workers and members of public are indicated. These locations are marked as A, B, C, and D ....etc. The exposure rates (mR) at these locations are measured under maximum scattering conditions for four cardinal gantry positions 0, 90,180 and 270 degrees (see table). The safety integrity of the installation is thus determined and found satisfactory.

b) Primary barrier adequacy

The primary beam is directed with fully opened apertures towards primary walls, ceiling and floor- the shielding adequacy of the primary barriers is measured (table-8)

DISCUSSION

After checking the equipment using the international protocols with regard to mechanical, optical and radiation systems a detailed radiation survey was conducted as per the standard procedures & practices laid down. The results thus obtained were sent to Atomic Energy Regulatory Board (AERB) Govt; of India, the competent authority for the country for approval. The certificates of approval was received and the equipment is now used for treatment of cancer patients.

FURTHER READING

1. Montague Cohen "Physical aspect of Teletherapy" AMPI Medical Physics Bulletin PP37-73(1986)
2. Khan F.M. Physics of Radiation Therapy Williams & Wilkins,London.

COVERAGE EVALUATION SURVEY OF IMMUNIZATION PROGRAMME IN HILLY AND PLAIN AREAS OF FIELD PRACTICE AREA OF GOVERNMENT MEDICAL COLLEGE SRINAGAR

M Rafiq MD, Sufoora Bilquees MD, M. A. Masoodi MD

ABSTRACT

We studied the immunization coverage in the field practice areas of GMC Srinagar i.e. in three blocks (Hazratbal, Ganderbal, and Lar) through a cross sectional study involving children <5 years old and pregnant ladies. The results revealed that OPV-0 was given to only three children .Fully immunized children were about 69.9% and partially immunized to be 30.1%. No case of non-immunized children was found. An insignificant relation between mother's educational status and full immunization was seen. Fully immunized pregnant woman were found in 50.9% while as partially immunized were found to 49.41% and non immunized about 7.81%. Immunization coverage in plain areas was 80.3% and 60% in hilly areas and the difference was statistically found to be significant. Most common reason for partial/non immunization was obstacles including child ill, family member busy or ill, vaccinator unavailable. Cold chain system analysis found vaccines at a proper temperature No temperature record of cold chain was kept at any place. Although standby generator facility was available every where yet it was not used during nights.

Conclusion: A system to rapidly identify partial/non immunized subjects is needed. Special sessions for special people like nomadic Gujjars need to established. Involvement of Private clinics will lead to a highly successful outcome.

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INTRODUCTION

India has a well developed schedule for immunization but adequate immunization coverage still remains an obstacle. In India, EPI (expanded programme of immunization) was launched in 1978. The Indian version of UIP was launched on November 19, 1985 and a National Immunization schedule was formulated. Measles incidence decreased since 1992 and polio is expected to be eradicated by 2005 AD with the help of pulse polio immunization. In 1993, Global Programs on vaccine (GPV) was launched with one of the aim to sustain high levels of immunization coverage. Success in UIP (Universal Immunization Programme) Led to launch of CSSM (Child Survival and Safe Motherhood) Program in 1992 and RCH (Reproductive Child Health) program in 1997 incorporating immunization as one of the major components[1]. In spite of immunization services available, everywhere they remain underutilized. Thus identifying the children, who were not age-appropriately immunized, became a public health priority. This vaccination survey helps us to give a true picture of vaccine coverage, cross checks the results, identifies other agencies providing immunization, identifies areas with good and poor coverage; determines age appropriateness of vaccines and identifies factors affecting it[2]

MATERIAL AND METHODS

While assessing the implementation programme of immunization being in force at state and national level, an assessment has been carried out in the field practice areas of Govt. Medical College Srinagar. For this purpose, a stratified random sample of 12 villages has been drawn from all the villages falling within the jurisdiction of three medical blocks namely Hazratbal, Ganderbal, and Lar. The frame constuted

Key words: Immunization coverage, hilly and plain areas, full immunization, dropout ra

two lists of villages in hilly and plain areas separately. With this stratification, four villages have been selected at random from each block, using two and three digit tables, two villages from hilly, and two from plain areas separately. Four proformas were initially devised to undertake the study, before being introduced in the field they were pretested, and necessary modification made wherever need arose. The reference period of the study being from 1st April 2000 to March 2001.In addition expectant mothers have been included for assessing the use of tetanus toxoid which being most important part of immunization.

All the families in the village were surveyed and inquiry was made from the household head regarding immunization of children (0-5 years) and of pregnant women. A family for the study was taken as one, were members shared the same kitchen and were blood related. In the household, all the members are not blood related e.g. servants or tenants[3]. Fully immunized child/pregnant lady were taken as one who had received age/gestational age appropriate vaccination. Partially immunization was taken as one who had received some immunization but it is not complete. Not immunized was taken as one where not even a single dose of vaccine has been received.[2] Immunization was confirmed from immunization card and wherever they were not available, the convincing history of immunization from mother as well as household head was taken as immunization. In the case of BCG, a scar was taken as immunization for the said vaccine.

Reasons for partial or non immunization was also recorded. Cold chain system was analyzed taking into consideration the requisite temperature as well as visual inspection.

OBSERVATIONS:

The population of the 12 villages sampled equaled to 17,063 comprising of 1772 house holds . All the selected villages have approach to the health unit and AWC are functioning in all these areas.

TABLE I. Statement showing distribution of sampled village surveyed by population and other related facilities

Block	Sampled village	Total HH	Population	Children < 5 years	Health unit	Edu. Instt.	Electricity	AWC	Terrain
GANDERBAL	1. BAMLOOR	167	1625	196	UD	High school	Available	Present	plain
	2. THURU	174	1500	192	PHC	Middle	-do-	-do-	Plain
	3. GUTLIBAGH	160	920	118	AD	Middle	-do-	-do-	Hilly
	4. SAIDPORA	125	1500	192	SC	Primary	-do-	-do-	Hilly
HAZRATBAL	1. DARA	124	1358	193	SC	Middle	-do-	-do-	Hilly
	2. NEW THEED	145	1783	253	AD	Middle	-do-	-do-	Hilly
	3. MALBAGH	122	1532	257	SC	Primary	-do-	-do-	Plain
	4. KRESHBAL	147	1230	311	SC	Primary	-do-	-do-	Plain
LAR	1. HARIPORA	144	1680	193	SC	Primary	-do-	-do-	Hilly
	2. WALIWAR	169	1625	211	SC	Primary	-do-	-do-	Hilly
	3. BARSOO	149	1300	240	SC	Middle	-do-	-do-	Plain
	4. ZARIGUND	146	1010	143	PHC	Middle	-do-	-do-	Plain
TOTAL		1772	17,063	2499					

Note : HH=household, UD=Unani Dispensary, PHC= primary health center, AD= Allopathic Dispensary, SC= Sub center. AWC= Anganwardi center

In all 2499 children, less than 5 years of age have been surveyed during the reference period of which 53% were males and 47% females. Immunization with respect of OPV, DPT, BCG, and measles besides Pulse Polio Immunization has been checked and has been placed in appropriate table. It is mentioned here that out of all the children only 6 children had been given OPV at birth that too in the hospitals where deliveries were undertaken.

TABLE 2. Distribution of children surveyed by age and sex

Age in years	Children male No.	%	Children female No.	%	Total No.	%
0-1.5	371	27.9	342	29.3	713	28.6
1.5-2.5	308	23.2	285	24.4	593	23.7
2.5-3.5	257	19.3	226	19.3	483	19.3
3.5-4.5	214	16.1	178	15.2	392	15.7
4.5-5	180	13.5	138	11.8	318	12.7
Total	**1330**	**100.0**	**1169**	**100.0**	**2499**	**100.0**

Immunization coverage under OPV/DPT by age and sex have been implicated in table no [3]. Under the national programme of immunization, DPT and OPV are simultaneously administered and as for as 1st dose is concerned, all the children of these areas have been benefited. Concerning the 2nd dose there is some decline and only 91.7% in male children and 88.8% in female children had been immunized. While administering the 3rd dose of DPT/OPV there is, further decline in immunization coverage. Among male children, 85.9% could be covered against 81.3% in females. As regards the booster dose, the coverage declined further as only 73.6% of the male children and 62.1% in female children received the booster with an overall immunization coverage of 71.83% irrespective of sex and it varied among different age groups from 56.89 to 82.70%. With regard to PPI (pulse polio immunization) on national immunization days there is 100% coverage as per information gathered. The requisite figures are tabulated in table II.

TABLE I. Immunization coverage under OPV and DPT by age and sex

Age in years	IMMUNIZATION COVERAGE OPV1andDPT1		OPV2 and DPT2				OPV3 and DPT3				BOOSTER (OPV and DPT)			
	both sex		male		female		male		female		Male		female	
	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
0-1.5	713	100.0	352	94.9	296	86.5	331	89.2	277	81.0	-	-	-	-
1.5-2.5	593	100.0	291	94.5	261	91.6	247	80.2	241	84.6	223	92.4	198	69.5
2.5-3.5	483	100.0	232	90.3	216	95.6	221	86	187	86.3	186	72.4	128	56.6
3.5-4.5	392	100.0	187	87.4	144	80.9	187	87.4	124	69.7	151	70.6	72	40.4
4.5-5	318	100.0	157	87.2	121	87.7	156	86.7	121	87.7	142	78.9	121	87.7
Total	**2499**	**100.0**	**1219**	**91.7**	**1038**	**88.8**	**1142**	**85.9**	**950**	**81.3**	**712**	**73.6**	**509**	**62.1**

TABLE II. OPV, DPT immunization and pulse polio immunization under national immunization programme and national immunization days (both sex combined)

Age in years	Total children surveyed	Immunization coverage National immunization programme OPV and DPT		National immunization day PULSE POLIO	
		NO.	%	NO.	%
0-1.5	713	574	80.50	713	100.0
1.5-2.5	593	421	70.99	593	100.0
2.5-3.5	483	314	65.01	483	100.0
3.5-4.5	392	223	56.89	392	100.0
4.5-5	318	263	82.70	318	100.0
Total	**2499**	**1795**	**71.83**	**2499**	**100.0**

Note: fall in immunization coverage due to OPV and DPT Booster missing

Dropout in subsequent doses 0f DPT/OPV is given in tableIII. The perusal of the figures exhibits that the dropout rate goes on increasing with increase in age of child i.e. from 0 to<5 years, with an interval of 1 year. The dropout rate fluctuates from 6.91 to 15.56% in OPV2 and DPT2 doses. While administering OPV3and DPT3, the dropout is 7.31% and varied between 0.36 to 11.59%. The highest dropout rate is marked while administering the booster dose. Overall, dropout rate comes to about 14.20% and varied from 5.50 to 28.3% in the different age groups.

TABLE III. Dropout rate in immunizing subsequent doses of OPV and DPT (both sexes combined)

Age in years	No. of children missing OPV2 & and DPT2	Dropout rate (%)	No. of children missing OPV3 and DPT3	Dropout rate (%)	No. of children missing booster dose of OPV and DPT	Dropout rate (%)
0-1.5	65	9.12	40	6.7	-	-
1.5-2.5	41	6.91	64	11.59	67	13.73
2.5-3.5	35	7.25	40	8.93	94	23.04
3.5-4.5	61	15.56	20	6.04	88	28.30
4.5-5	40	12.58	1	0.36	14	5.05
Total	**242**	**9.68**	**165**	**7.31**	**297**	**14.20**

TABLE IV: BCG and measles immunization coverage in children

Age in years	Immunization coverage											
	BCG						*MEASLES					
	Males		Females		Total		Males		Females		Total	
	No	%	No	%	No	%	No	%	No	%	No	%
0-1.5	364	98.1	330	96.5	694	97.3	153	88.4	152	84.0	305	86.2
1.5-2.5	304	98.7	279	97.9	583	98.3	305	99.0	278	97.5	583	98.3
2.5-3.5	255	99.2	221	97.8	476	98.6	256	99.6	222	98.2	478	99.0
3.5-4.5	214	100	170	95.5	384	98.0	214	100.0	178	100.0	392	100
4.5-5	180	100	138	100.0	313	100.0	180	100.0	138	100.0	318	100.0
Total	**1317**	**99.0**	**1138**	**97.3**	**2455**	**98.2**	**1108**	**97.9**	**968**	**96.0**	**2076**	**97.0**

Note: Of the total 713 children aged bellow 1.5 years, only 354 children i.e. 173 males and 181 females were eligible for measles immunization as such children bellow 9 months of age have been excluded while calculating percentage.

Table V: Immunization status in surveyed areas.

Age in years	Children immunized											
	Partially						Fully					
	Males		Females		Total		Males		Females		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-1.5	68	18.3	120	35.1	188	26.4.	303	81.7	222	64.9	525	73.6
1.5-2.5	85	27.6	87	30.5	172	29.0	223	72.4	198	69.5	421	71.0
2.5-3.5	71	27.6	98	43.4	169	35.0	186	72.4	128	56.6	314	65.0
3.5-4.5	63	29.4	106	59.6	169	43.1	151	70.6	72	40.4	223	56.9
4.5-5	38	21.1	17	12.3	55	17.3	142	78.9	121	87.7	263	82.7
Total	**325**	**24.4**	**428**	**36.6**	**753**	**30.1**	**1005**	**75.6**	**741**	**63.4**	**1746**	**69.9**

Note: Fully children stands far all those children covered under OPV, DPT, BCG, and measles and have been age appropriately immunized.

Table VI: Immunization status as per literacy of mother.

Literacy level	Total No. (%)	Fully immunized No. (%)	Partially immunized No. (%)	Total No. (%)
Literate Matric and above	148 (6.24)	109 (6.24)	40 (5.31)	149 (5.96)
Below matric primary, high schooletc.	258 (10.89)	174(9.97)	79(10.49)	253(10.12)
Illiterate	1964(82.87)	1463(83.79)	634(84.20)	2097(83.92)
Total	**2370(100)**	**1746(100)**	**753**	**2499(100)**

X2 value = 0.91 d.f. =2 p value insignificant at 5%
The result of the chi square test reveals that literacy and full immunization are not related

BCG and Measles immunization is presented in tableIV. While observing the tabulated figures, it is seen that BCG has been given to 98.2% of children, 99% in males, and 97.3% in females. As regards measles, there has been coverage of 97% in total with 97.9% in males and 96% in females. The coverage of measles in the age group greater than 3.5 years is seen to cent percent. There is under coverage bellow 3.5 years olds, which exhibits different response of people. The least coverage is seen in children who are in the age group of less than 1.5 years.

As regards immunization status in the surveyed area against all types of vaccines specifically, OPV, DPT, BCG. Measles is concerned; evaluation to this effect has been exclusively tabulated in table V. The table reveals that, 30.1% of the total children have been partially immunized and 69.9% have been fully immunized in respect of the above vaccines. Revealing this situation in different age groups, the coverage is very much fluctuating and no specific tendency is noticed with regard to response or coverage.

Immunization status as per literacy level of mother is shown in table VI. Perusal of the table shows that out of 1746 fully immunized children 1465 had illiterate mothers, while as 109 fully immunized children had mothers who were matriculate and above, 174fully immunized had mothers who were bellow matric. Partially immunized were more in illiterate mothers. Review the results as quoted above, it is observed that mothers who are matriculate or above appear to be more conscious regarding immunization of children as compared to other categories like who are bellow matric or just literate or illiterates. Applying chi-square test, the association between mothers literacy and full immunization was found to be insignificant at 5% level. It is thus inferred that literacy level did not have any significant relevance with the immunization programme.

Table VII shows distribution of pregnant women in relation to the gestational age. The total numbers of pregnant woman surveyed were 512, which accounts for about 3%. Evaluation has been made in relation to the 1st and 2nd dose of tetanus toxiod by gestational age. It is seen that 92.2% of the pregnancy cases were observed to have taken TT1, whereas only 50.6% of the total could approach for TT2. The average gestational age estimation at immunization and its coverage has been placed in tableVIII. The first dose has been taken on an average gestational age of 23.6 weeks where as the second dose has been taken at a gestational age of 27.95 weeks. The standard deviation and standard error of these estimates are shown in the table. 95% confidence interval about the average estimates exhibits that TT1 has been taken within the gestational age of 22.74 to 23.39 weeks and TT2 has been taken within the interval ranging between 27.67 to 28.23 weeks. Percentage of non-immunized cases as about 7.81%. 49.41% have been partially immunized. Complete immunization accounts for about 50.9%.

TABLE VII. Immunization status of pregnant woman by gestational age:

Gestational age in weeks	Pregnant woman		
	No. Pregnant woman (total)	1st dose of TT No. (%)	2nd dose of TT No.(%)
16-18	39	81 (17.2)	-(-)
18-20	25	36 (7.6)	-(-)
20-22	15	29 (6.1)	6 (2.3)
22-24	23	54 (11.4)	9 (3.5)
24-26	47	210 (44.5)	22 (8.5)
26-28	28	39 (8.3)	85 (32.8)
28-30	53	23 (4.9)	93 (35.9)
30-32	70	- (-)	44 (17.0)
32-34	133	- (-)	-(-)
34-36	79	- (-)	- (-)
Total	**512**	**472 (.100.0)**	**259 (100.0)**

Note : (-) dash stands far nil.

Table VIII. Estimation of average gestational age at immunization and coverage.

Estimation particulars	Immunization of pregnant woman	
	TT Ist (weeks)	TT2nd (weeks)
A. i. Average gestational age	23.06	27.95
ii. Standard deviation	± 3.54	± 2.23
iii. Standard error	± 0.16	± 0.14
iv. 95% confidence limits	(22.74-23.39)	(27.67-28.23)
B. i. % coverage of immunized cases	92.19%	50.59%
ii.% Of unimmunized cases	7.81%	

The immunization assessment in the experimental area appeared to be satisfactory. In reviewing the present situation, prevalent in whole of the province it was felt necessary to observe how for these programme have been carried in hilly areas which comparatively involves difficult terrain especially under cold climatic conditions. The comparison of immunization status in children in hilly areas and plain areas is presented in table IX.

TABLE IX. Comparison of immunization status in hilly and plain areas

Age in years	Children fully immunized					
	Hilly areas			Plain areas		
	Total children	No. immunized	%	Total children	No. immunized	%
0-1.5	395	241	61.0	318	284	89.3
1.5-2.5	285	189	66.3	308	232	75.3
2.5-3.5	260	126	48.5	223	188	84.3
3.5-4.5	185	104	56.2	207	119	57.5
4.5-5	158	110	69.6	160	153	95.6
Total	**1283**	**770**	**60.0**	**1216**	**976**	**80.3**

1. *Proportion* $p_1 = 0.600$ $p_2 = 0.803$
2. *Standard error* $SE_1 = \sqrt{0.000187}$ $SE_2 = \sqrt{0.00013}$
3. Proportion difference/standard error difference
   p1-p2 = 0.203 SE (p1-p2) = 0.0178
4. Ratio = p1-p2/ SE (p1-p2) = z z = 11.178

Highly significant $p < 0.01$

Result: *Due to highly significant differences in coverage in hilly and plain areas it is inferred that coverage is better in plain areas than in hilly areas It reveals that only 60% of the children have been fully immunized in hilly areas as compared to 80.3% in plain areas. The difference being highly significant as displaced on application of statistical test. It is inferred that immunization coverage in plain areas is defiantly better than in hilly areas and the reason is obvious.*

Regarding reasons for non/ partial immunization it was observed that all those who had slight knowledge about immunization had positive attitude towards availing immunization programme but the shortfalls, which appear to have hindered in utilizing these services has been placed in Table X.

Table XI. Reasons for partial immunization of children in the study area

S no	Reason of partial immunization	Total	%(n=100)
1.	Wrong ideas and notion about immunization contraindications like child ill	(n=753) 304	40.37
2	Mother was busy	227	30.15
3	Vaccinator absent	57	7.57
4	Conflict in the area where it was thought better to stay at home	52	6.90
5.	Others	113	15.00

Note : others include non availability of vaccine, no faith in vaccination etc

As regarding partial immunization in pregnant woman: wrong ideas and notion about immunization was the main reason

TABLE XI: inspection of vaccine carrier from airport to regional level

VACCINE	CONTAINER		REGIONAL COLD STORAGE	
	Position	Temperature	Type	Temperature
OPV	Filled with ice cubes	-	DEEP FREEZER	-20°C
Measles	-do-	-	DEEP FREEZER	-20°C
BCG	-do-	-	WIC/ILR	+2°C
DPT	-do-	-	WIC/ILR	+2°C
TT	-do-	-	WIC, ILR	+2°C

Note WIC stands far walk in cool room, ILR stands far ice-lined refrigerator

TABLE XII. Secondary level inspection

Vaccine network distribution network	Vaccine storage system	Temperature record						Visual inspection like for VVM, etc
		OPV *	DPT	BCG	Measles *	DT	TT	
WELL Baby clinic (SMHS Hospital)	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
Lal Ded Hospital	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
Children Hospital	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
PHC Hazratbal	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
PHC Ganderbal	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
PHC Lar	Deep freezer	-15°C			-15°C			Satisfactory
	ILR, Refrigerator		+2°C	+2°C		+2°C	+2°C	
Dispensary	3 day carrier	-	-	-	-	-	-	Satisfactory
AWC	3 day carrier	-	-	-	-	-	-	Satisfactory
Immunization site	3 day carrier	-	-	-	-	-	-	Satisfactory

*NOTE: * these alone have been kept in deep freezer-hence the temperature*

VVM stands far vaccine vial monitor and other inspection is far freezing and thawing

Govt Medical College Srinagar collects the quota of vaccines directly from regional stores so as to avoid any intermediary storage system. Deep freezers as well as ice lined refrigerators (ILR's) as well as refrigerators are used at the well baby clinic, Lal Ded hospital, Children hospital and at all PHC's. Only at dispensaries as well as at sub centers, AWC's and other immunization posts are three day carrier or one day carrier used for carrying as well as providing vaccines. Since they do not have a storage system, the unused vaccines are brought back to the PHC. At all levels efforts have been made to check the temperature which actually exist within the vaccine storage system, so the data could not be collected in them. The requisite data is placed in table XI and XII. Visual inspection of vaccines was also made and this was noticed to be satisfactory.

DISCUSSION:

Kashmir is situated entirely in the Himalayan region and is northern most state of the country. It is a cold region with the seasonal temperatures varying from -10 0C during winter and 350C in summers. The present study was undertaken in all the three blocks representing the field practice areas of the Govt. Medical College Srinagar namely block Hazratbal, Ganderbal and Lar. These blocks have village strength of 128, 96, and 55 with the population of 98108; 91503 and 49993 respectively. Out of which 12 villages have been randomly selected with a population of 17063 that makes about 7.11% of total study population

The above mentioned sampling method was used for evaluation since it was felt that 30-cluster sampling method routinely used by WHO although cheap, simple, and reliable with a confidence interval of 90%, yet does not allow for comparison between different clusters. In addition, it does not identify small clusters with poor performance[4]. The study is restricted to a population of 12-23 months and done in restricted period. Besides a large number of health, workers are needed for such studies.[2]

Of the 2370 total families in the study area, 2499 children were enumerated. An average of 7.6 members was found per household. Munshi IH (1988)[5] found it to be 7.7 members per household in an earlier study in Ganderbal block of Kashmir. Regarding concern about family, size which in demography is said to be total number of children a woman has born at a point of time[6] no comment can be made from our study since only children 0-5 years were enumerated and as such not compared with the average The total children studied were 2499, which forms 14% of the population and coincides with the 1991 census of India. The male children accounted for about 53% as against 47% female children. This reflects an overall national figure, which has been adverse to females. The reason being the social customs wherein a female child is considered inferior to males and thus getting discrimination because of prenatal sex determination. They are also being considered as a temporary resident who are to be married off and hence getting lesser health care. OPV-0 was given only to six children in the entire study population accounting for about 0.24%. The national immunization coverage figure of OPV-O is about 30% as per MOHandFW evaluation of routine immunization coverage for year 1997-98[7]. However, NFHS-2[8] survey reports the figure of only 13% for the OPV-0 coverage in the whole country. The worst situation as per the present study reflects the lower number of hospital deliveries in the block. Fazilli A (2000)[9] had reported institutional deliveries in about 6.25 % in the urban areas of Hazratbal bock of Srinagar city. However, the present study area is predominantly rural with an equal representation for hilly area where the deliveries are conducted mostly at home. One of the reasons for this being that the institutions in the area is open only during 10am to 4pm. Although a few centers in the experimental bock work round the clock, still the immunization facility is not available after 4 pm with the delivered woman getting discharged early in the morning without vaccinating her child.

The coverage for OPV, DPT first dose (OPV/DPT1) was about cent percent in the study area. Salhotra VS (1999)[10] showed it to be 82.64% in his study area. Banera SK (1999)[11] reported coverage of 66% in Orrisa. Singh P (2000)[12] reports a national figure of 87.6% The figures in our study reflect on the impact of awareness about immunization in children especially in newborns, wherein the massive campaign during pulse polio immunization (NID's) has already helped the attitudes and practices regarding immunization.

The coverage for DPT/OPV2 in males and females was found to be 91.7% and 88.8% respectively. Salhotra VS (1999) and Banera SK (1999) reports it to be 84.3%and 51.2% respectively in their study areas. Singh P (2000) reports a national figure of 84.7%. The high figure from the present study reflects again on the sustained immunization campaigns launched during pulse polio immunization.

As for as coverage of OPV/DPT3 is concerned, the coverage is about 83.6%. Salhotra VS (1999) reports it to be 70.5% respectively in his study areas.. As per WHO report (2000)[13] the overall national coverage is about 78% and as per NFHS-2 survey (1998-99) the coverage for rural area of JandK is 90%. These figures coincide with that of the present study.

Pulse polio immunization coverage overall was to the tune of about 100% in the study area. NFHS-2 (1998-99) survey reports it to be 97.2% for the year 1997-98 for JandK. Singh P (2000) reports a national average of 96.8%. Kumar R (2001)[14] reports these figures to be about 96% for Haryana. These high figures are due to sustained IEC activities, mobilization of opinion leaders, and also because of launch of intensified phase of PPI wherein house to house search is made and the child immunized at his residence also.

Dropout between doses was calculated which ranged from 6.91 to 15.56% between OPV/DPT-1 and OPV/DPT-2. As for as dropout between OPV/DPT2 and OPV/DPT3 is concerned, it is about 7.31%. The low dropout between OPV/DPT2 and OPV/DPT3 in our study is because of better immunization awareness of people created by the sustained NID's (National immunization days) activities. The dropout between OPV/DPT3 and booster doses is very high. The overall dropout was seen to be about 14.20% (5.50-28.3%). This high dropout for the booster dose can be explained by the fact that repeated immunizations on NID's has created an impression among some people that the booster is not needed since the child is already getting the dose.

BCG coverage is about 98.2% in the present study. Salhotra VS (1999) records the coverage to be about 74.80%. WHO 2000 global summary reports a national coverage of about 80% for the whole country while as NFHS-2 reveals an all India level of about 72%. The high coverage is attributed to the fact that the block under study are being run by Govt. Medical College Srinagar, wherein the field staff is regularly monitored for their immunization activities. In addition, pulse polio immunization has also created an attitude wherein every newborn infant are not neglected from the programme. However a slight under coverage in the age group of 2.5-3.5 years cannot be explained, may be the conflict in the area had a role..

The overall measles coverage was noticed to be about 97%. NFHS-2 survey conducted in the year 1997-98 reveals the coverage to be about 97% in the age group of 12-23 months in the urban poor of Srinagar city, 93% in the age group of 24-35 months and 16% in the age group of 6-11 months.

About 69.9% of the children in the experimental area were fully immunized, 30.1 % of children in the age group of 0-5 years were found to be partially immunized. No un-immunized child was noticed in the experimental area. AS PER NFHS-2, survey the figures for JandK for fully immunized children stands at about 60-79%. Salhotra VS (1999) in their study areas found fully immunized children to be 58.26% ,while as partially immunized to be about 25.21% respectively, the remaining accounting for non immunized. The absence of non- immunized children in the study area speaks about the health awareness of people boosted by the NID's campaign. This campaign has also given our health workers an opportunity to advocate routine immunization.

An insignificant association between mothers educational status was seen with full immunization in the present study. More concern about immunization of children with literate mothers was seen. Viswanathan and Rhode (1990)[15] found that fully immunized children were more in those whose mothers were literate. A good percentage of full immunization is seen in illiterate mothers in the present study and this is because of sustained IEC activities regarding pulse polio immunization and regarding child health. As per coverage evaluation survey of 1997-98 by MOHandFW Govt. of India the full immunization coverage was 68% in age group of 24-35 months and 60% in age group of 12-23 months when both parents were literate.

As for as pregnant woman are concerned about 512 such woman were identified and enumerated in the experimental blocks, which accounts for about 3% that is slightly less than the national average. The marginal decrease is because of hiding of pregnancy especially in primis because of social customs and taboos.

98.2% of pregnant woman were seen to have benefited from TT1, while as about 50.6% had received TT2 or booster Fazilli A (2000) reported a coverage of about 40.6% in the Hazratbal block for TT2/ Booster that is consistent with the present study.

It was seen that TT1 was taken at an average gestational age of 23.6 weeks while as TT2 was taken at gestational age of 27.95 weeks. For TT1 it ranged from 22.74-23.39 and for TT2 it ranged from 27.67weeks to 28.23 weeks. These figures show gestational age appropriateness of immunization in the study area as recommended wherein the first dose is given at a gestational age of 16-24 weeks or at the first contact of the woman and second given after a gap of one month preferably one month before delivery[3]

A highly significant difference between hilly and plain areas was noticed with 80.3% of overall immunization in the plain areas and 60% in the hilly areas. Zaffar A et al (1996)[16] found that there was significant difference between immunization coverage in the urban, non-tribal and tribal areas with a low percentage in tribal areas. Hilly areas in the present study mostly consist of tribal population and our figures coincide with the same report.

The present study found that the reasons for partial immunization were mainly due to obstacles in the immunization despite the majority having good attitude and motivation. The main reasons in the obstacles include: child ill, family members - busy or ill, vaccinator unavailable because of Hartals, conflict in the area. Bhattarcharjee (1993)[17] reports obstacles constituting about 39.06% of reasons for failure of immunization

The cold chain system in the study area was found to be effective, vaccines being kept at a proper temperature and that the visual inspection in terms of VVM was found to be satisfactory. Although electricity failures occur frequently during winter yet the temperatures drop appears to be protective against them. Grasso M (1999)[18] reports that out of 52 primary vaccinations offices in central Italy, 76.5% had a refrigerator for vaccine storage but only 33.3% kept records of received and stored doses. They found that none of these centers had maximum and minimum thermometer and that none monitored the internal temperature of refrigerator. They also found that vaccines were kept in door shelves that showed inadequate knowledge of health workers. Similar observations were considered here, however no drawbacks in the cold chain system were noticed, and health workers dealing with the vaccines were well trained and fully aware about the system. However, temperature maintainence records were not seen to have been kept.

CONCLUSION AND RECOMMENDATIONS

Although this is small study in comparison to the vast dimensions of country's immunization programme and its findings cannot serve as a basis for generalization nevertheless these findings do strongly point to the necessity of undertaking similar evaluations in other parts of JandK and in different types of health settings and facilities. .In this connection the following recommendations are made:- Assessment and feedback of immunization performance should be made whose purpose would be to alert health providers to the actual coverage and motivate them to improve coverage. In this connection, strategy of AFIX adopted by Georgian Public Health Clinics (USA) to improve immunization coverage should be used. This strategy is a short abbreviation for Assessment, Feedback of results, Incentives for improved performance in the form of community recognition, plaques and or dinner rather than financial incentives and Exchange of information to stimulate competition. Those who are not immunized, a reminder should be given with a computerized tracking system to better identify and follow defaulters. Parents should be given a booklet about the immunization, the doses, intervals between doses and efficacy of vaccines. Establish a continuing medical education for health workers especially involved in immunization. A system to identify rapidly non-immunized or partially immunized children so that they could be provided with immunization as early as possible. Optional vaccines should be introduced into national immunization programme like hepatitis B, Varicella vaccine and Hib vaccines.

Combination vaccines should be introduced to decrease dropouts. Cold chain should be monitored regularly with technicians available for repair of defunct refrigerators. Special immunization clinics should be established for people with special problems like nomadic Gujars moving from one place to another. A national childhood vaccine injury act with appropriate compensation should be implemented on the pattern of US so that people get faith in the system. Private clinics should be involved in the immunization campaign and they should be monitored regularly.

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ADVANCE TRAUMA LIFE SUPPORT

Purpose, history and concepts

Tariq Sheikh *

COMMENT

Advance trauma life support provides with a safe, reliable method for immediate management of the injured patient and the basic knowledge necessary to:.

1. Assess the patient's condition rapidly and accurately.
2. Resuscitate and stablize the patient accordingly to priority.
3. Determine if the patient's needs exceed a facility's capabilities.
4. Arrange appropriately for the patient's inter hospital transfer (what, who, when and how)
5. Assure that optimum care is provided.

OBJECTIVES

1. To orient medicos to the initital assessment and management of the trauma patient.
2. To assist doctors in providing emergency care for the trauma patient.

GOLDEN HOUR

The concept of "golden hour" emphasizes the urgency necessary for successful management to maximize outcome of the injured patien and is not intended to imply a 'fixed' time period of 60 minutes. A doctor must have the essential information and skill to apply for the indentification and treatment of life threatening or potentially life threatening injuries.

A doctor or a paramedic after having completed ATLS course should be able to:-

A. Demonstrate concepts and principles of primary patien assessment.
B. Establish management priorities in a trauma situation.
C. Initiate primary and secondary management necessary within the "golden hour" for the emergency care of acute life threatening emergencies.
D. Demonstrate in a given simulated clinical and surgical skill practicum the following skills used in the initial assessment and management of patients with simulated, multiple
    i. Primary and secondary assessment of a patient with simulated, multiple injuries.
    ii. Establishing a patent airway and initiating one and two person ventilation.
    iii. Orotracheal and nasotracheal intubation on adult and infant.
    iv. Pulse oximetry and CO_2 monitoring.
    v. Cricothyroidotomy.
    vi. Assessment and management of the patient in shock including initiation of percutaneous venous access and recognition of life threatening haemorrhage.
    vii. Venous cut down (optional).
    viii. Pleural decompression via needle theracentesis and chest tube insertion.
    ix. Pericardiocentesis.
    x. Identification of thoracic injuries (X-ray)
    xi. Evaluation of abdomen (USG, CT) (peritoneal lavage).
    xii. Head and neck trauma assessment and management (Glasgow coma scale)
    xiii. Identification of spine injuries (X-ray).
    xiv. Identification of intracranial lesions.
    xv. Neuro trauma evaluation.
    xvi. Musculoskeletal trauma assessment and management.

NEEDS

As tragic as in any "accidental" death, the loss of life in the early years is the most tragic. Research money spent on communicable disease e.g., Polio, Diphtheria has nearly eliminated the incidence of these diseases. The disease of trauma has not captured the public attention in the same way. Methods and modalities are available to prevent most injuries but unfortunately public awareness has not translated into public utilization and acceptance e.g., helmets and seat belts. It is the failure of the public utilization and acceptance which makes the knowledge of ATLS more necessary.

HISTORY

A new approach to the provision of care for individuals suffering major life threatening injury premiered in 1978. The first ATLS course was conducted early that year. In 1979 the Committee on Trauma (COT) of American College of Surgeons (ACS) recognizing trauma as a surgical disease adopted the course under the impromatur of the college and incorporated it as an educational program.

Before 1980, even in USA, the trauma care by doctors was inconsistent. There was a drastic change after a tragedy took place in Feb. 1976 when an orthopaedic surgeon, piloting his plane, crashed in rural Nebraska Comifield The surgeon sustained serious injuries, three of his children sustained critical injuries and one child sustained minor injuries. His wife was killed instantly. The care, he and his family received was inadequate by the day's standards. Recognizing the inadequate treatment, the surgeon stated, "When I can provide better care in the field with limited resources than what my

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children and I received at the primary care facility there is something wrong with the system and the system needs to be changed."

A group of private practice surgeons and physicians in Nebraska, Lincoln Medical Education Foundation and the Lincoln area mobile heart team nurses with the help of the university of Nebraska Medical Centre, the Newbraska state committee on trauma of the ACS and South east Nebraska Emergency Medical Services identified the need for training in ATLS. The first prototype ATLS course for doctors was a combined educational format of lectures, associated with life saving skill demonstrations and practical laboratory experiences.

The original intent of the ATLS programme was to train doctors who do not manage major trauma on a daily basis. However, today the ATLS method is accepted as a standard for the first hour of trauma care by many who provide care for the injured, whether the patient is treated in an isolated rural area or a State - Of - The - Art trauma centre.

TRIMODAL - DEATH DISTRIBUTION

Death due to injury occurs in one of three time periods.

1. First peak.
2. Second peak
3. Third peak

FIRST PEAK

Death occurs within seconds to minutes of injury. Death usually result from laceration of brain, brain stem, high spinal cord, heart, aorta and other large vessels. Very few of the patients can be salvaged due to the severity of their injuries. Salvage after injury during this peak can be achieved only in certain large urban areas where rapid pre-hospital care and transportation are available.

SECOND PEAK

Death occurs within minutes to several hours following injury. The ATLS primarily focuses on this peak. Deaths during this period are usually due to subdural and epidural haematomas, haemopneumothorax, ruptured spleen, lacerations of liver, pelvic fractures and / or other multiple injuries associated with significant blood loss. The "first hour" of care after injury is characterized by the need for rapid assessment and resuscitation which are the fundamental principles of ATLS.

THIRD PEAK

Death occurs several days to weeks after the initial injury. Death is often due to sepsis and multiple organ failure. Care provided during each of the preceding periods impacts on patient outcome during this stage.

CONCEPT

The approach to the injured patient as being taught in the medical colleges was the same as that for a patient with a previously undiagnosed medical condition i.e., present history, past history, and physical examination from top to bottom. This approach might be adequate for Medical patients or even many acute surgical illnesses, but it certainly did not satisfy the needs of the patient suffering from life threatening injury. Therefore, the approach required change.

THREE CONCEPTS OF ATLS

1. The most important concept is to treat the greatest threat to life first.
2. Secondly the lack of a definitive diagnosis should never impede the application of an indicated treatment.
3. The final concept was that a detailed history was not essential to begin the evaluation of an acutely injured patient.
   The result was the development of the "ABCDEFG" approach to the evaluation and treatment of the injured.

"A" Airway and cervical spine protection.
"B" Breathing.
"C" Circulation - control external bleeding.
"D" Disability or neurological status.
"E" Exposure (undress) and environment (temperature control).
"F" Fractures.
"G" General condition

The ATLS course emphasizes the rapid initial assessment and primary management of the injured patient, starting at the time of injury and continuing through initial assessment, life saving interventions, re-evaluation, stabilization, and when needed, transfer to a trauma centre. The ATLS course is intended to provide the doctor with one acceptable method for safe, immediate management and the basic knowledge necessary to:

i. Assess the patients condition rapidly and accurately.
ii. Resuscitate and stabilize the patient according to priority.
iii. Determine if the patient's needs exceed a facility's capabilities.
iv. Arrange appropriately for patients inter hospital or intra hospital transfer.
v. Assure that optimum care is provided.

INTERNATIONAL DISSEMINATION

ATLS programme was exported outside of North America in 1986 to the Republic of Trinidad and Tabago. The ACS Board of Regents gave permission in 1987 for promulgation of the ATLS programme in other countries within strict guidelines.

TRIAGE

Triage is the sorting of patients based on the need for treatment and avialable resources to provide the treatment based on ABC priorities. It also patients to the sorting of patients in the field and the need for facility to which they are to be transported. Two types of triage situations usually exist.

A) MULTIPLE CASUALITIES

The no. of patients and the severity of their injuries do not exceed the ability of the facility to render care. In this situation, patients with life threatening problem and those sustaining multiple system injuries are treated first.

B) MASS CASUALITIES

The no. of patients and the severity of their injuries exceed the capabilities of the facility and staff. In this situation those patients with the greatest chance of survival with the least expenditute of time, equipment, supplies and personal are managed.

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* The author has worked in the critical care units in Iran (1983-1995) and Sandia Arabia (1997-2001)

Review

[illegible] MANAGEMENT OF [illegible]

[illegible] M.D., [illegible]

D.M., Ph.D.

[illegible] The [illegible] clinical description [illegible]

[illegible] meningitis [illegible]

[illegible] Robert Whytt [illegible]

[illegible] Koch in [illegible]

[illegible] tuberculosis [illegible]

[illegible] the Tuberculous [illegible]

[illegible] complication [illegible]

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[illegible] IN TUBERCULOUS [illegible]

of the immunocompetent [illegible]

[illegible] can be [illegible]

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[illegible] Blindness [illegible]

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TBM reduces fatality rate (43% vs 59%). Moreover they also showed that the neurologic complications after initiation of therapy (4 vs 10) and permanent sequelae were also lower in the dexamethasone treatment group.

Similarly Schoeman DF et al[6] showed that corticosteroid significantly improves survival rate and intellectual outcome in TBM as they cause an enhanced resolution of basal exudates and tuberculomas. But they failed to show a dramatic effect of steroids on the ICP due to hydrocephalus[4,6].

Dexamethasone in a dose of 0.2 mg/Kg/day in 3-4 divided doses via parenteral route or prednisolone in a dose of 1mg/Kg/day is given for 4-6 weeks and then gradually tapered over a equal period of time[13].

Diuretics such as frusemide may be given in a dose upto 1mg/Kg/ at 6-8 hour interval by the oral, IM or IV route with an average adult dose of 40 mg at 8 hour interval. Injection mannitol may be used in life threatening situations or a critical rise in ICP. Acetazolamide in a dose of 100 mg/Kg/day in 3 divided doses in often required for therapy with an average adult dose of 250 mg, twice or thrice a day. Continued therapy with frusemide and acetazolamide may decrease CSF production for few days but do not cause ventriculomegaly to resolve instead causes a rebound increase in ICP[15].

SURGICAL THERAPY

Hydrocephalus being a common complication of TBM it is suggested that once ventriculomegaly sets in, surgical drainage is the only effective way of reducing raised intracranial pressure[11].

SURGICAL OPTIONS

☐ Ventricular tap
☐ Ventricular shunt
☐ Endoscopic third ventriculostomy

VENTRICULAR TAP

This procedure is indicated when a shunt cannot be placed immediately due to poor general condition of patient, lack of operative facilities and concurrent pyogenic infection. However, if offers advantages like:

☐ Helps in assessing CSF pressure and defining the role or indication of surgery.

☐ Provides CSF sample for diagnostic study.

☐ Fastest in reducing intracranial pressure, but it improves the clinical condition only for 6-8 hours hence, repeated tapping is therefore needed till the patient is favourable for shunt surgery. Complications like infection, intraventricular bleeding, bleeding along the track, pneumocephalus, poren cephalic cysts along line of ventricular puncture and localized brain damage may occur.

Endoscopic third Ventriculostomy (ETV)

A percutaneous or stereotactic ETV creates an opening in the floor of the third ventricle to alleviate hydrocephalus. It can be used in cases where the CSF is obstructed at the level of the aqueduct or distal to it[15]. A success rate of 40-60% has been reported in the setting of post tubercular hydrocephalus.

SHUNT SURGERY

Shunt surgery is often needed in patients with TBM who develop hydrocephalus. While some workers have managed early hydrocephalus with anti-tubercular therapy (ATT) without surgery, others advocate shunt placements in all patients with hydrocephalus[28].

TIMING FOR SHUNT SURGERY

Kemaloglu S et al[29] showed that early surgical procedure for mild/moderate hydrocephalus has a positive effect on the morbidity and mortality of hydrocephalus in childhood TBM. Moreover, in severe hydrocephalus, early shunting have a positive effect on morbidity. However, in several patients diversion of ventricular CSF doesn't improve their clinical condition and may die despite the intervention[30,31]. Some researchers have proposed selection of patients on the basis of staging of tubercular meningitis. As hydrocephalus rarely develops in stage I and II TBM indication for shunt surgery is low here[16] whereas a shunt is mandatory for all grade III or IV patients with attendant hydrocephalus[32]. From a prognostic point of view altered sensorium (grade III) is a better stage to put the shunt rather than waiting for decerebration to occur (grade IV)[11].

CRITERIA FOR SHUNT SURGERY

1. Clinical[11]

Symptomatic hydrocephalus with one or more of the following signs and symptoms:

☐ Persistent headache and vomiting
☐ Papilloedema/optic atrophy
☐ Decreased level of consciousness
☐ Gait ataxia or progressive neurological deficit
☐ Decerebration / Decortication

2. Neuro-imaging[11]

☐ CT/MRI/evidence of active hydrocephalus i.e. ventriculomegaly with periventricular lucency (PVL) or edema.

3. CSF Criteria[11]

☐ Cellcount- CSF polymorph count should be less than 5/cm3 irrespective of the number of lymphocytes.

☐ A protein content of less than 100 mg/dl is no longer required or considered mandatory for shunt surgery.

4. Ventricular tap criteria

☐ Evidence of raised ICP and a significant fall in the ICP along with clinical improvement following the ventricular tap, is a definitive indication for performing a surgery.

METHODS AND RESULTS

CSF shunts divert CSF from the ventricles into the body cavities. Of the various shunt options available a ventriculo peritoneal shunt (VP) is the most accepted procedure for hydrocephalus. Venticulo-atrial shunts (VA) have a higher complication rate and therefore not preferred[15,16]. Choice of shunt is based on cost, availability and intraventricular pressure. Putting up a low pressure device in high ventricular pressure hydrocephalus would result in over drainage syndrome. Similarly a high pressure device will not drain hydrocephalus with low or moderate intraventricular pressure[16]. Connection is maintained between a burr hole created behind the ear where the tip is placed in the frontal horn of the right lateral ventricle and the peritoneal connection is often placed in the epigastrium or in the right upper or lower quadrant after being tunneled subcutaneously across the chestwall[32].

Alleviation of increased ICP after shunt may result in improvement in sensorium within 48-72 hours. A postoperative CT is advised in all cases ideally by 1 week after shunt surgery or earlier if there is clinical deterioration or no improvement. The CSF parameters may take months to normalize[33,34]. The CSF glucose returns to normal within 2 months in 50% of the patients and within 6 months in the majority. The CSF cellular response takes almost 6 months to normalize in approximately 25% cases, whereas CSF protein remains elevated for more than 6 months in 40% cases.

COMPLICATIONS

The overall complication rate of shunt surgery is about 20%[32]. Common complication includes shunt obstruction and infection. Others include hematoma, hemiparesis, seizures, shunt migration/disconnection/fracture, Peritonitis, Peritubal leakage/shunt excoriation, overdrainage, endocarditis, nephritis[16,32].

Shunt malfunction may develop within 7 days due to shunt misplacement or shunt blockage by blood clots and fibrin debris[16]. Patient have symptoms like headache, vomiting, drowsiness which may appear, disappear and recur again with increasing frequency and severity[15]. Patency of the shunt is confirmed by clinical method, transcranial Doppler (TCD) study and CT and MRI imaging. Delayed onset malfunctioning occurs after 7 days[16] due to infection, shunt migration or plugging of the catheter by choroid plexus or the peritoneal catheter by omental adhesions. 5 to 10% of shunts are complicated by infection[15] caused by S. epidermidis (60%) and S. aureus (30%) cases. The remainder is caused by coliform bacteria, streptococci or Hemophilus influenza[15].

OUTCOME

Although morbidity rates reported may be as high as 88%-100% despite shunt surgery[14] but still with effective procedure neurologic improvement following ventricular decompression may be dramatic particularly in children with improvement in the level of consciousness and other signs and symptoms[13]. Daljit Singh et al11 showed that only 60.3% of patients with grade III and 34.5% of patients with grade IV showed improvement following ventriculo-peritoneal shunt surgery whereas the improvement rate was 100% for group I and II TBM patients11. Palur R et al[28] found that the mortality rates in grade III and IV were 51.9% and 100% respectively, despite a policy of early shunt surgery of all patients. John M Mathew et al[14] suggested a trial for an external ventricular drainage as a preliminary procedure for grade IV patients who has otherwise a poor prognosis with shunt surgery. They suggested that all patients of grade III should be given the benefits of shunt surgery without a trial of external ventricular drainage but poor outcome for grade IV patients (88% mortality) underlines a need for them to undergo a trial with external ventricular drainage and response to the drainage of CSF to determine the necessity or otherwise of shunt surgery.

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PHOTOCHEMOTHERAPYAND ITS VARIANTS: SAFE AND USEFUL MODES OF THERAPY

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Before going into the discussion of photochemotherapy and its variants it is necessary to understand the basic terms and concepts used in relation to it. Phototherapy ['photos' meaning 'light'], as the name suggests, means the use of sunlight or any other source of light as a treatment modality in any human ailment. A simple example of phototherapy is the use of sun exposure or artificial blue light in the treatment of neonatal jaundice. The term photochemotherapy differs from the former in that a chemical substance or drug is used here in addition to the light exposure, the light exposure being essential for the drug to act. A classical example of such a therapy is the PUVA [psoralen and UV-A light] therapy, useful in a number of cutaneous as well as systemic disorders. Another variant of phototherapy is the photodynamic therapy [PDT] in which a photosensitizing chemical is used either topically or systemically and it is then excited by sunlight or some other artificial light source to cause the destruction of the target tissue. Many benign as well as some premalignant and malignant skin lesions can be safely and effectively treated by this mode of therapy. A recently introduced variant of phototherapy is what is known as Extracorporeal Photopheresis [ECP], which is basically a combination of phototherapy and leukopheresis. Here selective irradiation of the leukocyte or buffy coat fraction of the blood is done outside the human body [extracorporeally] in presence of a psoralen.

HISTORY OF PHOTOCHEMOTHERAPY

Photochemotherapy using plant extracts and subsequent exposure to sunlight as a form of treatment in vitiligo has been used since ancient times, as early as 1500 BC in India and Egypt[1]. However, the first scientific use of phototherapy dates back to 1948 AD when Fahmy et al. in the University of Cairo, isolated three chemical compounds from the fruit of a plant Ammi majus. They named these three compounds as Ammoidin [8-methoxypsoralen], Ammidin and Majudin [5-methoxypsoralen] [1]. El Mofty from the same institution documented the use of these chemical substances as successful treatment options in vitiligo[2]. Lerner in 1953 further documented the role of psoralen photochemotherapy in patients with vitiligo[3]. The first synthetic psoralen, Trimethylpsoralen [TMP] was introduced in 1964 and has been used ever since especially in the treatment of vitiligo. The modern form of photochemotherapy using high intensity UV-A sources was first introduced at the Harvard-Massachusetts General Hospital Dermatology Laboratories[4]. The concept of extracorporeal Photopheresis [ECP] was introduced in 1987[5] as a treatment option for cutaneous T cell lymphoma [CTCL]. The first use of photodynamic therapy [PDT] in humans is credited to von Tappeiner who, in the year 1907, treated human skin tumors effectively by applying a 5% solution of eosin dye followed by exposure to sunlight[6].

PHOTOCHEMOTHERAPY [PUVA THERAPY]

Psoralen administration with exposure to UV-A light or PUVA therapy [P=psoralen; UVA= ultraviolet A light] is the most popular and widely used form of photochemotherapy. The therapy usually consists of oral administration or topical application of a psoralen followed by exposure to ultraviolet-A light [320-400nm wavelength] at a time when the concentration of the psoralen in the tissues is adequate. The psoralen in the tissues gets activated by the UV-A light and then acts on its target molecules especially the DNA.

Key words: Phototherapy, Photochemotherapy, Photopheresis, PUVA, Photodynamic therapy

PHARMACOLOGY OF PSORALENS

Psoralens are tricyclic furocoumarin compounds found naturally in certain plant species or synthesized in vitro. The three most commonly used psoralens are 8-methoxypsoralen [8-MOP] or Methoxsalen; 5-methoxypsoralen [5-MOP] or Bergapten and 4,5,8-trimethylpsoralen [TMP] or Trioxsalen. The trimethyl derivative is not found naturally and is only synthesized in vitro. It is also less phototoxic than 8-MOP when used orally.

When used orally psoralens are absorbed from the gastrointestinal tract and this absorption is dependent upon many factors namely the formulation of the drug, coexistent food intake, first pass effect in liver and also inter-individual differences in absorption. The formulation of the psoralen affects its absorption in a big way, liquid preparations getting absorbed much more than crystalline ones[7]. Co-existent food intake also decreases and delays the absorption of the psoralen and first pass metabolism in the liver also affects the total amount of drug reaching the blood[8]. It needs to be emphasized that this first pass metabolism in the liver is saturable so that a small increase in the oral dose can lead to an unexpected rise in the blood levels of the drug[9]. On the other hand a really small dose of the drug gets totally metabolized in the liver and no appreciable quantity of the drug reaches the blood. Inter-individual differences in absorption also occur and this accounts partly for the rare cases not responding expectedly to PUVA therapy in the usual doses[9].

After absorption psoralens get distributed to almost all tissues and are excreted in the urine mostly as metabolites within an average of 12 hours. Peak levels of psoralens in the blood after oral intake are seen after 1-8 hours with a mean of 2 hours[8]. This forms the basis for giving UV irradiation after two hours of oral intake in PUVA therapy.

When psoralens are applied topically they rapidly penetrate the skin and can be detected in the urine after about 4 hours. The plasma levels of 8-methoxypsoralen [8-MOP] after whole body application are comparable to those found after oral administration of the drug[10]. However, with bath-water PUVA the plasma levels of the drug attained are negligible, around 1% of those seen with oral PUVA[11].

The mechanism of action of psoralens is not fully understood. However two possible mechanisms are described[12]:

1. Direct method [Type 1]: Psoralens are believed to form photoadducts with Thymine and Cytosine bases of DNA in presence of ultraviolet light leading to inhibition of DNA synthesis and thus cell proliferation. A direct effect on amino acids in the cells and lipoproteins is also postulated.
2. Indirect method [Type 2]: Psoralens also act indirectly by forming reactive oxygen species in presence of ultraviolet light. These reactive oxygen species then cause damage to DNA, destruction of membrane bound Cytochrome-P450, oxidation of membrane lipoproteins and also activation of Cycloxygenase pathway.

Psoralens act much more on cells that are actively dividing than on resting cells as is expected from the mechanism by which they exert their effect on the cells. This explains why they are effective only in the active stage of scleroderma and not in the fibrotic stage. Action on actively dividing or activated immune cells especially T lymphocytes explains their action in immune mediated diseases like psoriasis, lichen planus, graft versus host disease, granuloma annulare etc. In vitiligo, a stimulatory effect on melanocytes secondary to action on c-AMP pathway is postulated.

FUNDEMENTALS OF PUVA THERAPY

The main aim of PUVA therapy is to bring about a controlled, persistent phototoxic reaction. For this purpose UV-A exposure is given, usually from broadband, high intensity UV-A sources having an action spectrum between 320 and 380 nm. When solar irradiation is used instead of an artificial UV-A source, the therapy is called as PUVASOL therapy ['SOL' for solar]. A major disadvantage of PUVASOL therapy is that the UV exposure cannot be quantified and the total amount of UV-A reaching the skin does not remain constant, varying with the season, time of the day, latitude and condition of the atmosphere.

In case of oral PUVA the drug is given usually on an empty stomach and the patient is exposed to UV-A light after 1-3 hours, the initial UV-A dose determined either by skin typing [See Table 1] or by phototoxicity testing. In case of phototoxicity testing the patient's minimal phototoxic dose [MPD] is first calculated and this usually forms the initial dose of UV-A exposure. Minimal phototoxic dose [MPD] is defined as the least possible dose of UV-A that causes a barely perceptible erythema of skin in an individual patient. The UV-A dose is then sequentially increased as per the protocol followed [European, American or any other]. The frequency of UV-A exposure is either three or four times per week and this frequency of treatment is usually continued till the patient goes into remission. After attaining remission, especially in immune mediated diseases like psoriasis, lichen planus etc. the frequency of exposure is then reduced and the last UV-A dose is continued during the maintenance therapy. The duration of this maintenance therapy depends upon the disease being treated and its propensity to relapse.

With topical treatment the psoralens rapidly penetrate the epidermis, within approximately 10 minutes in normal skin and presumably faster in psoriatic skin[13]. Thus there is no need to wait for 1 or 2 hours for the UV-A or solar irradiation after topical application of psoralens. Frequency of treatment remains the same as in oral PUVA i.e. about 3-5 times per week. Dose increments in case of topical PUVA/PUVASOL have to be made gradually and have to be tailor-made for each individual patient. This is because topical PUVA has a propensity to cause adverse phototoxic reactions, seen in the form of intense erythema or blistering of exposed skin. In fact, this adverse reaction is the most important limitation of topical photochemotherapy.

BATH WATER PUVA

It is a novel method of delivery of psoralens to the skin that shows an efficacy equal to that of the oral method[14]. In this method the patient is immersed in a bathtub filled with a dilute solution of 8-methoxypsoralen [8-MOP] for about 20

Skin type	Characteristics	Initial dose of UV-A
Skin type 1	Always burns, never tans	0.5 joules/cm^2
Skin type 2	Always burns, sometimes tans	1.0 Joules/cm^2
Skin type 3	Sometimes burns, always tans	1.5 joules/cm^2
Skin type 4	Never burns, always tans	2.0 joules/cm^2
Skin type 5	Moderately pigmented [Brown]	1.5 joules/cm^2
Skin type 6	Deeply pigmented [Black]	3.0 joules/cm^2

Table 1: Skin types and the initial UV-A exposure

minutes followed immediately by exposure to UV-A light. The psoralen solution is made by dissolving 5-to50 mg of 8-methoxypsoralen in each 10 liters of water. Several factors make bathwater PUVA the most popular method of PUVA therapy. The treatment is less messy as compared to topical treatment, a short 15 minutes bath is sufficient for any patient, the psoralen gets evenly distributed over the patient's skin and thus leads to even repigmentation in vitiligo, the gastrointestinal side effects are totally avoided and a smaller dose of UV-A exposure is needed to achieve the desired effect. The systemic side effect profile also gets dramatically reduced with bath-water delivery and the photosensitivity after each dose does not last for more than two hours, thus there is no need for the patient to avoid UV exposure after receiving the dose[14].

Bathwater PUVA has been increasingly used as a form of photochemotherapy in the last few years and studies have documented a far less incidence of adverse reactions with this mode of treatment. The risk of cutaneous malignancies has also been claimed to be less with this form of photochemotherapy[15]

BATH-SUIT PUVA

It is a variant of bath-water PUVA that has been used in India. Bathtubs in India are not in vogue and most of the patients, being from the poor class, cannot afford bath-water PUVA. In such circumstances bath-suit PUVA has proved to be a cheap and effective alternative[12,16]. Advantages of bath-suit PUVA include:

a) Only two liters of water and 0.8 ml of 8-MOP solution are needed compared to about 100 liters of water and 50 to 500 mg of 8-MOP in case of bath-water PUVA.

b) Treatment can be continued even at home with sunlight as the UV-A source.

c) Cost of treatment is far less as compared with bath-water PUVA.

d) Systemic side effects of oral PUVA are not seen.

Disadvantages of bath-suit PUVA are:

a) Head and neck does not come in contact with the drug-thus not effective in lesions on head and neck area.

b) Concentration of drug in the bath-suit may not be uniform.

INDICATIONS AND CONTRAINDICATIONS OF PUVA

PUVA, which was confined to the realm of vitiligo therapy in the past, finds its use in a number of cutaneous and systemic diseases at present. The disorders in which PUVA therapy has been used till date include:

SKIN DISORDERS

1. Psoriasis especially in cases with >20% body surface area involvement
2. Vitiligo
3. Cutaneous T-Cell lymphoma
4. Cutaneous Mastocytosis
5. Lichen planus
6. Atopic eczema
7. Morphea
8. Prevention of photosensitive disorders like polymorphic light eruption [PMLE], solar urticaria, chronic actinic dermatitis etc.
9. Pityriasis rosea
10. Alopecia areata
11. Nodular prurigo
12. Persistent palmoplantar pustulosis
13. Chronic graft-vs-host disease
14. Histiocytosis X
15. Dermatitis Herpetiformis
16. Miscellaneous disorders like Pityriasis rubra pilaris [PRP], pityriasis lichenoides chronica, lymphomaoid papulosis etc.

OTHER DISORDERS

1. Systemic Sclerosis
2. Scleromyxedema
3. Mixed Connective Tissue Disease [MCTD]

Contraindications include:

1. Pregnancy and lactation
2. Severe liver disease
3. Renal failure
4. Xeroderma pigmentosum
5. SLE or Porphyrias
6. Personal or family history of melanoma

SIDE EFFECTS OF PUVA

PUVA is considered to be a well-tolerated therapy with minimal incidence of serious side effects. The side effects

5. Keratoacanthoma
6. Condyloma acuminata
7. Kaposi's sarcoma
8. Psoriasis
9. Miscellaneous conditions like nevoid basal cell carcinoma, cutaneous metastasis etc.

SYSTEMIC DISORDERS

1. Carcinoma bladder
2. Esophageal carcinoma
3. Lung carcinoma
4. Macular degeneration

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SCENARIO

Ishfaq Ahmed

ABSTRACT

marker for suicidal risk.

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study by the lead author(19) showed that 16.76% of the population had had suicidal ideations and 2.47% of them which works out to approximately 1.5 lack people belonged to high risk group. Keeping in view the emergent disturbing trends on one hand and controversial relationship of serum cholesterol level with suicide on the other the present study was undertaken with two main questions in mind. First to find out whether there is any difference in serum cholesterol level of the attempted suicide patients and second is there an association between serum cholesterol level and the sudden spurt in suicidal attempts being increasingly reported over the past few years in Kashmir(2-5,19-21)

MATERIAL AND METHODS:

All 50 consecutive cases of suicidal attempt admitted in the emergency services of the general hospital (SMHS) of the government medical college Srinagar from 1st January 2000 were studied as the index group. Three groups of age and sex matched 50 subjects in each group were included as the controls in the study for engaging into multiple comparisons .One control group comprised of consecutive 25 patients of depression without any suicidal behavior and 25 patients of generalized anxiety disorder attending the psychiatry OPD at the same general hospital. They were diagnosed on the basis of DSMIV criteria. The other control group comprised of minor medical illnesses mostly acid peptic disorder cases attending the medical OPD adjacent to psychiatric OPD. The third control group comprised of normal volunteers among the 7th semester MBBS students. Both these groups were screened by psychiatric interview and none of theme met the criteria for any psychiatric disorder. Informed consent was obtained from all subjects after an explanation of the study procedures. Specially designed semi structured

TABLE I. Socio-demographic Characteristics of the index and control groups:

Variable	Index Group	Psychiatric Control	MMA Patients	Normal Control
1. Gender:				
Male:	17(34%)	12(24%)	5(10.2%)	12(24.4%)
Female:	33(66%)	38(76%)	44(89.8%)	37(57.14%)
2. Age (in years)				
0-20	23(46%)	17(34%)	4(81.6%)	14(28.57%)
21-35	25(50%)	22(44%)	43(87.75%)	32(65.3%)
Above 35	02(4%)	11(22%)	2(4.08%)	03(6.13%)
3. Economic Class:				
Upper:	9(18%)	01(2%)	4(8.16%)	12(24.49%)
Middle:	31(62%)	23(46%)	35(71.43%)	35(71.43%)
Lower:	10(20%)	26(52%)	10(20.41%)	02(4.08%)
4. Marital Status				
Unmarried:	41(82%)	26(52%)	10(20.41%)	49(100%)
Married:	07(14%)	24(48%)	39(79.59%)	-
Divorced:	02(4%)	-	-	-
5. Family status:				
Nuclear:	27(54%)	22(44%)	18(36.73%)	27(55.10%)
Joint:	23(46%)	28(56%)	31(63.27%)	22(44.89%)
6. Level of education:				
Graduates:	10(20%)	12(24%)	9(18.36%)	-
Undergraduates:	21(42%)	11(22%)	12(24.49%)	49(100%)
Illiterates:	19(36%)	27(54%)	28(57.15%)	-
7. Occupation:				
Students:	28(56%)	16(32%)	-	49(100%)
Housewife:	19(38%)	17(34%)	27(55.10%)	-
Govt. Employees:	02(4%)	9(18%)	22(44.90%)	-
Others:	01(2%)	8(16%)	-	-
8. Social Class				
Rural:	44(88%)	43(86%)	41(83.67%)	43(87.76%)
Urban:	6(12%)	7(14%)	18(36.73%)	6(12.24%)

TABLE II: Diagnostic Break up in each of the four subjects group

Normal Index	Psychiatric Control	MMA Patients
Normal	Depression 14(28%)	APD 40(100%) 25(50%)
	Depression with Psychotic features 01(02%)	
25(50%)	Generalized anxiety disorder / Depression with PTSD 06(12%)	
	Personality disorder 06(12%)	
	No apparent Psychiatric illness. 11(22%)	
	Accidental ingestion. 07(14%)	
	Drug ingestion 04(08%)	
	Suicidal gesture 03(06%)	
	Panic disorder 02(04%)	

TABLE III: Serum lipid profile of subjects belonging to various groups

Group	Triglycerides (mg/dl) Mean	S.D	SEM	Cholestrol (mg/dl) Mean	S.D
Index Group	110.74	3.7	31.12	146.41	4.
Psychiatric Control	150.58	4.3	12.64	179.7	4.
MMA Patients	179.68	4.4	14.52	181.63	4.
Normal control	151.25	3.0	10.81	169.83	4.
HDL				LDL	

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TABLE II: Diagnostic Break up in each of the four subjects group

Normal Index Psychiatric Control MMA Patients
Depression 14(28%) 25(50%)
Depression with Psychotic features 01(02%)
Generalized anxiety disorder 25(50%) Depression with PTSD 06(12%)
Personality disorder 06(12%)
No apparent Psychiatric illness. 11(22%)
Accidental ingestion. 07(14%)
Drug ingestion 04(08%)
Suicidal gesture 03(06%)
Panic disorder 02(04%)

TABLE III: Serum lipid profile of subjects belonging to various groups
Cholestrol (mg/dl) Triglycerides Mean S.D SEM
Index Group 3.7 31.12 146.41
Psychiatric Control 4.3 12.64 179.7
MMA Patients 4.4 14.52 181.63
Normal control 3.0 10.81 169.83
HDL LDL

Performa was used to record the socio demographic data, present history, past history of suicide attempt, family history, medical history, dietary history and physical examination. Exclusion criteria including use of contraceptives, pregnancy, lactation, substance use and presence of medical illness like hypertension, coronary heart disease, diabetes mellitus, hypothyroidism, nephrotic syndrome, liver disorder and familial hyperlipidemia Routine blood investigations blood sugar, blood urea, serum creatinine, serum bilrubin were done in all subjects and those with abnormal tests were excluded from the study. Blood samples were obtained in the morning after the subjects had had over night fast. Blood was obtained from ante-cubital vein and total serum cholesterol, triglyceride, HDL levels were determined using merkotest kit by enzymatic method and serum LDL was determined by Friedewald's equation (22).

STATISTICAL ANALYSIS

Comparison between continues variables in the matched groups were made using the analysis of variance (ANOVA) for paired samples. Variables were then entered into backward step wise multiple regression analysis within each group, the association of lipids as a continuous variable with variables of interest was estimated using Pearson's correlation coefficient for continuous variables and the two-sided t test for categorical variable. Factors significant on univariate analysis were entered into a backward stepwise multiple regression model to determine independent factors. Next the indexed group was examined with each controlled group separate using backward stepwise logistic regression.

RESULTS

In the current study various groups were taken into consideration among which table I contains the sociodemographic characteristics of the index and controlled groups. The index group comprised almost exclusively of acute suicidal poisoning with 76% cases belonging to organophosphorus poisoning alone. Table II presents the diagnostic break up of study subjects. Table III contains serum lipid profile of subjects belonging to various groups included in the study. Table IV gives the statistical analysis of data.

DISCUSSION

As a result of the present study we seem to have found some answers to our two principal questions. A significant difference was observed in the mean cholesterol and triglyceride levels among the four groups. The suicidal group had the lowest($p<.001$) and the non psychiatric controls the highest level with psychiatric control group falling intermediate between non psychiatric controls and the normal controls though the lower mean cholesterol in the suicidal attempt group accords with some other previous studies(23,24) but what is striking here is that unlike many other reports the mean triglyceride level was also lowest in these subjects. This raises the question that in addition to other psychosocial predisposing factors is the present continued strife with increasing socioeconomic hardships among the masses leading them to excessive austerity measures resulting in underfeeding and consequent low serum lipids? If so, then in our speculative and unproved view this might be one of the significant factors responsible for sudden spurt in suicidal attempts from mid 90,s onwards against long standing patterns of very rare incidence of suicidal attempts in Kashmir. Had the recent phenomenon of highly increasing incidence of suicides been only the direct immediate effect of the violence as claimed in some reports (5) then suicidal rates should have been same if not more during the early 90,s which was not in any way less threatening and less uncertain than the present times. Dietary amino acid tryptophan which is the precursor of serotonin-a neurotransmitter whose deficiency is known to induce depression, suicidal tendencies and aggressive behaviors can get depleted up to the 85% if excluded from an oral load of mixture of amino acids(25). This aspect has also been part of our investigation but will be reported separately. Our conjuncture of adverse socioeconomic conditions contributing biologically also to the increase in suicidal rates finds support from the overrepresentation of the subjects (82%) from lower and lower middle socioeconomic background. A higher percentage of suicidal attempt cases (66%) comprising mostly of young females in addition to other reasons may also support the above reason as female gender in general and young women in particular continue to be discriminated in the society especially among lower socio economic groups to which most of these cases belonged. However universally observed phenomenon that also needs to be considered in the context of this higher female ratio is that independent of country or culture there is a two fold greater prevalence of depressive disorder in women than in men(26). Reasons hypothesized for this difference include hormonal differences and the effects of childbirth besides differing psychosocial stressors and behavioral models of learned helplessness in women. Another reason for this over representation from the lower strata of the society may be that people belonging to higher socioeconomic class usually try to avoid public health institutions not only because of their preferred private treatment seeking behavior but also to avoid medico legal procedure and social stigmatization following suicidal attempt by a member of their family or group. As is clear from the diagnostic breakup of the index group in table II ,the largest subgroup (28%) belongs to depressive disorders with one case of co morbid psychosis and another one with co morbid PTSD. This is in complete agreement with the previous observation that major depression is one of the most important risk factors for suicide(27). Since majority of depressive cases in general population even in most advanced places like USA are assumed to receive little if any treatment(28,29) therefore the state of affairs can be well imagined at a place like ours with ever-increasing number of psychiatric disorder in general (30) and depressive disorders in particular(31)on one hand and non existent community based treatment services on the other. The need to improve the diagnosis as well as quality of care with continuous follow up in the treatment of depression seems evident (32). In order to prevent suicides in general population. Despite the close association of mood disorders with suicidal behavior and the remarkable awareness in medical treatment of major psychiatric

[illegible]

adernergic one or still other to an agent that acts on both serotonergic or non adernergic transporter(64). A recent study investigating relationship between cholesterol level and depressive disorder on a sample of depressive disorder patients with none of the cases having attempted suicide, reports that serum cholesterol serum triglycerides and serum LDL were significantly lower in definite suicidal committers compared to partial committers. Another recent study in a sample of 100 cases revealed that 62% of cases that had attempted suicide had mild or moderate depression only. Furthermore much less is known about how the effects of psychotropic drugs translate into antisuicidal clinical response(65). Evidence is mounting that genetic factors may be included in the many determinants of suicide(52). Recently molecular genetic studies report that polymorphism of tryptophan hydroxylase gene that is involved in the synthesis of serotonin is associated with suicidal behavior(66). The psychiatric disorder or environmental stress, may serve as a potentiating mechanism that fosters or triggers an under lying biological susceptibility suicidal behavior.(52) It will therefore be quite pertinent for the future research to investigate whether the same underlying molecular mechanism manifests itself in the psychopathology and symptom otology including suicidal behaviors in common psychiatric conditions like depression ,PTSD, ,drug abuse and schizophrenia or there is a distinct bimolecular and genetic mechanism for suicide irrespective of the psychiatric syndrome with which it may be associated .

Besides inherent limitations of so many confounding factors affecting serum lipids the extra details about the present suicide scenario in Kashmir in this article is to initiate a process of overcoming the extreme paucity of relevant scientific data on suicides in Kashmir and to stimulate further debate and discussion on this vital issue among the local colleagues for whom this part of the paper is specially intended.

One more limitation of our study is that all most all the cases in our index group belonged to the sub group of acute suicidal poisoning cases only as this has been the suicidal patient profile in this general hospital over the years(3,4).Cases adopting more violent suicidal methods like slitting throat, Jumping strangulating or use of fire arms are not represented in this sample.

Our findings conclude lower serum cholesterol concentrations among suicidal attempters are consistent with some other recent studies (67,68) of similar nature but to the best of our knowledge aware the present study is the first of its kind comparing suicide attempt cases including suicidal depressive disorder patients with depressive disorder patients without any suicidal behavior. It can be suggested that low serum cholesterol level may serve as a biological marker for suicidal behavior irrespective of psychiatric morbidity as most of the recent studies have not been able to find out any specific relationship between low cholesterol and common psychiatric ailments like depression but a strong inverse relationship has been found between serum cholesterol level and suicidal attempts.

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CLINICAL PROFILE OF TUBERCULOUS MENINGITIS IN KASHMIR

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ABSTRACT

Tuberculous meningitis is the most life threatening form of extra pulmonary tuberculosis and was uniformly fatal before the advent of antituberculous chemotherapy. A two-year hospital based study was conducted, wherein seventy six patients of tuberculous meningitis were diagnosed, treated and followed. Patients were subjected to clinical examination and investigations like ESR, Mantoux test, CSF analysis, ELISA for IgM antibodies in CSF and serum and CAT scan of brain. It was observed that tuberculous meningitis is most common in the age group of 20 to 39 years, mostly among females. 52.6% patients were symptomatic for more than 4 weeks. Past history of tuberculosis was elicited in 7.89% cases. The most common clinical presentation was fever, headache, vomiting, altered sensorium, various cranial nerve palsies and papilloedema. Radiological evidence of active pulmonary tuberculosis was seen in 39.47% patients. Combination chemotherapy with 4 drugs for one year was found most effective regimen. Hepatitis was the frequently encountered drug induced complication. Morbidity and mortality was higher in stage III of disease, extremes of age and with delay in initiation of treatment.

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INTRODUCTION

Tuberculosis is a chronic infection caused by mycobacterium tuberculosis, characterized by cell mediated hypersensitivity and formation of caseous granulomas(1,2). CNS involvement accounts for 5-10% of the cases of clinical tuberculosis(3). In the central nervous system (CNS) tuberculosis, meningeal involvement is the most common followed by spinal tuberculosis. In the order of frequency, pathological changes are seen in meninges, ependyma, choroid plexus, blood vessels and brain parenchyma (4,5).

Tuberculous meningitis presents as acute meningitic syndrome, an insidious subacute demyelinating process or tuberculous encephalopathy. Factors adversely effecting the outcome include extremes of age, malnutrition, associated miliary tuberculosis, presence of underlying debilitating diseases, hydrocephalus, evidence of high intracranial tension, hypoglycorrhacia, very high CSF protein (6) and pregnancy(7). To know the clinical profile of TBM, a two year hospital based study was conducted in Kashmir valley during 1996 to 1997.

MATERIAL AND METHODS

This study was carried out on hospitalized patients at S.K Institute of Medical Sciences, Srinagar which is a specialty oriented, 600 bedded hospital in Kashmir Valley and serves an indigent population of 3.6 million. Seventy six patients were evaluated, treated and followed for a period of two years. Patients were grouped into 3 stages according to severity of illness at presentation as per the criteria of modified British Medical Research Council(8).

Stage I: Nonspecific symptoms, conscious, few or no clinical signs of meningitis.

Stage II: Signs of meningitis, drowsy, cranial nerve palsies.

Stage III: Stupor or coma, systemic toxicity, paresis or paralysis.

Clinically suspected cases of tuberculous

Key words: Tuberculous meningitis (TBM), Cerebrospinal fluid (CSF), CAT Scanning, Combination chemotherapy.

meningitis were investigated to support the diagnosis of TBM as follows:

i. Routine tests, ESR, liver function tests, chest X-ray PA view.

ii. Specific investigations: Mantoux test, Ziehl-Neelson stain sputum, urine, aspirate from lymph node and CSF, CSF analysis for cells, biochemistry, serum and CSF for ELISA for IgM antibody using A60 antigen and a CAT scan of brain.

All 76 patients were treated with antitubercular drugs, isoniazid, rifampicin, pyrazinamide and ethambutol or streptomycin for first 2 months. Isoniazid and rifampicin were continued for a period of 10 to 16 months determined on case to case basis. Steroids (prednisolone 1 mg/kg body weight or dexamethasone 0.2mg/kg body weight per day) were used in patients with stage II and stage III disease for a period of 2-4 weeks and tapered over an equal period of time (9,10). Patients were followed for residual physical or mental deficit for 2 years.

Statistical evaluation was done using Chi-square test and P-value calculated, using student's t-test.

RESULTS

Fifty eight (76.31%) patients belonged to rural areas of the valley. Forty two (55.26%) patients were in the age group of 20 to 39 years and females outnumbered males. Forty (52.63%) patients presented with symptoms of greater than 4 weeks and one had symptoms of 6 months duration. Six patients (7.89%) had past history of pulmonary tuberculosis and eight (10.52%) had family history of pulmonary tuberculosis. Symptoms and signs noticed at presentation were as depicted in Table 1.

Thirty eight (50%) were in stage II disease and thirty (39.47%) in stage III. Elevated ESR was found in sixty two patients (81.57%) in 1st hour, anemia in thirty patients (39.47%) and lymphocytosis in sixteen patients (21.05%). Mantoux test was positive in forty two patients (70%) out of sixty in whom this test was possible. Thirty patients (39.47%) had abnormal chest X-ray, revealing diffuse miliary infiltrates in sixteen(21.05%), apical infiltrates and fibrosis in two each, pleural effusion, cavitary shadow and mediastinal adenopathy in one each. Acid fast bacillus (AFB) was negative on smear of sputum, urine and aspirate in all cases. Twenty two patients (28.94%) had CSF leucocyte count of more than 200 cells/mm3 and thirty six (47.36%) had CSF lymphocyte count of greater than 90%. CSF glucose of less than 60% of corresponding blood glucose was found in fifty six patients (73.68%) and less than 70mg /dl in sixty patients (78.94%). Thirty eight (50%) had CSF proteins of 51-100mg/dl. ELISA for IgM antibody against A60 mycobacterial antigen was positive in thirty two (42.10%) and forty six (60.52%) patients for serum and CSF respectively. Abnormal CAT Scan findings were observed in fifty patients (73.53%) out of sixty eight in whom it was possible.

All the patients received antitubercular treatment (ATT). Isoniazid, rifampicin, pyrazinamide and ethambutol or streptomycin for first 2 months and isoniazid and rifampicin for rest of period with pyridoxine. Eight patients in Stage I and thirty eight patients in stage II received 12 months treatment and thirty patients in stage III received 18 months treatment. Steroids were given to sixty eight patients who were in stage II or III disease. Ten patients needed ventriculoperitoneal (VP) shunt surgery in addition to ATT. Six patients in stage III died. Drug induced hepatitis was seen in ten patients. The neurological disabilities like cranial nerve palsies were found in twenty four patients and ten were left with sequelae after treatment. Amenorrhoea, galactorrhoea, diabetes insipidus, decerebrate posturing was seen in two patients each.

CAT Scan has prognostic importance also. Brain edema, basal enhancement, infarcts and hydrocephalus are reported to have a bad prognosis (11). We also correlated abnormal CAT Scan findings with the outcome. Out of six deaths, three had hydrocephalus two had basal enhancement and one had brain edema. Patients who presented with illness of greater than 4 weeks had sequelae of TBM. Mortality was higher in age group of less than 20 years and above 70 years.

DISCUSSION

Tuberculous meningitis is seen with a high prevalence among infants and children in developing countries. However in more developed nations, tuberculous meningitis is now frequently seen in adults and elderly in association with reactivation or late generalized tuberculosis. The HIV pandemic also has been associated with increased case rates of CNS tuberculosis. 5 to 10 % of HIV infected patients with tuberculosis have CNS involvement predominantly as meningitis(12-15).

Maximum patients belonged to rural areas of the valley and were mainly poor, illiterate and ignorant. Forty two patients (55.26%) were in the age group of 20-39 years. The higher percentage of adults can be explained on the basis that for pediatric patients, there is a separate referral center in the valley. Females (60.2%) out numbered males which is explained by the fact that females are more illiterate, poor and under privileged. Most common symptoms reported at presentation were of greater than 2 weeks duration(16,17). However our forty patients had symptoms of greater than 4 weeks. Slightly greater duration of symptoms could be attributed to difficult access to specialized medical centers. Past history of tuberculosis could be elicited in 7.89% of cases which is in accordance with the literature. Fever, headache, vomiting, altered sensorium, cranial never palsies and papilloedema are the most common signs observed(16-18). Similar observations were made in our study.

Lumbar puncture and examination of CSF formed cornerstone of diagnosis in our series. The fluid is usually clear or ground glass in appearance. CSF glucose of less than 40mg/dl in 32% to 88% of patients, elevated protein level, and a lymphocytic pleocytosis with 100 to 5000 cells/mm3 is reported(17). We observed a total white cell count of greater than 200 cells/mm3 in 28.97% cases. CSF lymphocytosis of greater than 90% was seen in 51.44% cases. CSF glucose of less than 60mg/dl and protein of 75mg/dl was found in 78.96% and 73.68% patients respectively. Thus we

Table 2

Showing Symptoms and Signs in TBM

No.	Symptoms and signs	No. of patients	Percentage(%)
1.	Fever	64	84.2
2.	[illegible]	[illegible]	[illegible]
3.	Vomiting	48	63.15
4.	Signs of meningeal irritation	[illegible]	[illegible]
5.	Altered sensorium	[illegible]	[illegible]
6.	Anorexia	30	39.4
7.	Cranial nerve palsy	[illegible]	[illegible]
8.	Papilloedema	[illegible]	[illegible]
9.	Neurodeficit (limb weakness)	14	[illegible]
10.	Abnormal movements	[illegible]	[illegible]
11.	Convulsions	14	[illegible]
12.	Chest signs	4	[illegible]

[illegible]

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CLINICO-PATHOLOGICAL PROFILE OF CARCINOMA ESOPHAGUS AND ESOPHAGOGASTRIC JUNCTION IN KASHMIR

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ABSTRACT:

A total of 680 patients (390 males and 290 females) with carcinoma Esophagus and Esophagogastric junction, treated at the Department of Radiation Oncology of SKIMS Srinagar from year 1992 to1995, were analyzed retrospectively to study the clinical profile, pathological features and response to treatment modality used. The study revealed that 90% of patients presented with dysphagia to solids. Majority of the lesions were squamous cell carcinomas. The main modality of treatment used was External Beam Radiation. The overall survival at 1, 2 and 3 years was 15.4%, 10% and 4.4% respectively.

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INTRODUCTION:

Carcinoma esophagus is the seventh most common cancer worldwide. It is fairly uncommon in the United States, representing only 7% of all gastrointestinal malignancies and less than 2% of all malignancies(1). It is responsible for approximately 12,000 deaths annually in the United States(2). An International geographical belt exists, where carcinoma of esophagus is endemic and is termed "Asian Esophageal Cancer Belt," around the Caspian Sea(3). Yet an unrecognized fact in geographic pathology is that, cancer of the esophagus has the highest incidence in India - particularly noted in Assam, West Bengal, Andhra and Maharashtra(4,5). It is the most common cancer seen in Kashmir. The incidence rate of this disease as reported by some investigators was 22.6 per 100,000 population in men and 11.5 per 100,000 in women(5), whereas, the age adjusted incidence rate of cancer of esophagus per 100,000 population in Bombay is 10.2 in males and 10.6 in females(3). The overall results of treatment of carcinoma esophagus and esophagogastric junction have remained extremely poor, despite advances in surgery, radiotherapy and chemotherapy(6). Because of the late onset of symptoms, delays in patients' presentation, early lymphatic and hematogeneous dissemination and close neighborhood of esophagus to adjacent structures, majority of patients present with loco regional unresectable disease or with established metastasis at the time of diagnosis(7 8). 51% of patients who come to hospital are in no state to receive any treatment due to advanced disease, 32% qualify for curative therapeutic attempts and in 17%, only palliation is possible(4).

This study presents a retrospective clinico- pathological analysis of 680 patients, seen at Sher-I-Kashmir Institute of Medical Sciences, Srinagar (SKIMS) during the period 1992-1995. We also attempted to define various treatment modalities used, and outcome of therapies, and finally to emphasize on the seriousness of the problem that esophageal cancer poses in Kashmir.

MATERIAL AND METHODS:

A total of 680 patients with histopathologically documented esophageal and esophagogastric junction carcinomas were registered in the department of Radiation Oncology SKIMS Srinagar, during the period, January 1992 to December 1995. Evaluation of the patients included - detailed history, physical examination, blood count, liver and renal function tests, X-ray investigations including barium

Key Words: Carcinoma, Esophagus Esophago-gastric junction, External Beam Radiation

swallow esophagus, ultra sonogram abdomen, upper G.I. endoscopy and biopsy. Each case was studied in detail to determine the pattern of disease at presentation, treatment, clinical course and eventual survival. External beam irradiation was the main treatment modality performed, All 680 patients were subjected to Radiation therapy on Theratron 780 (Cobalt 60) Unit, for a tumor dose of 40-60Gy. Initial 40Gy was delivered by two parallel opposed portals (Ap/PA) over a period of 4 weeks using one fraction per day for 5 days a week. After a gap of 2-3 weeks, a boost of 20Gy was delivered by one anterior and two posterior oblique portals at a rate of 2Gy per fraction per day in two weeks. 57 out of 680 patients received adjuvant chemotherapy after radiation therapy of 40Gy. Out of 57 patients, 25 received single agent chemotherapy (5 FU-500mg/m2 i/v bolus), 12 received Methotrexate -50mg/m^2, Iv short infusion),14 received Cisplatin- 50mg/m2 I/V infusion over 3 hours plus Methotrexate 50mg/m2 I/v short infusion over 30 minutes and 06 patients received 5FU - 500mg/m2 I/v bolus, bleomycin 15 units I/v bolus plus etoposide 100mg I/V infusion over 2 hours and Methotrexate 50mg I/v short infusion. Combination chemotherapy was a single day regimen, and cycle was repeated 3 weekly and 3-4 such cycles were given. Since patients had presented in an advanced stage, only 04 patients during this period underwent primary resection of the tumor with esophago-gastric anastamosis, using thoraco- abdominal approach. The length of the follow up was measured from the first day of radiation therapy and a median follow-up of 3-48 months was available.

RESULTS:

The 680 patients studied, included 390 males and 290 females, ranging in age, from 40-70 years (Table 1). Most common presentation was dysphagia to solids (90 %.) Other symptoms in association with dysphagia included loss of appetite (80%); generalized weakness (70%); weight loss (50%); retrosternal discomfort/pain (40%) and vomiting/regurgitation (20%).

Morphologically, the gross lesion of the tumor was ulcerative, infiltrative and polypoid in 24.5%, 20.14% and 16.17% of cases respectively (Table 2).

35.58% of the patients had tumor located at 26-30 cm level in the esophagus from incisor teeth (Table3)

629 patients had squamous cell carcinoma (92.51%), while 50 (7.35%) patients had adenocarcinoma and 01 patient (0.14%) had oat cell type of carcinoma (Table 4). So for as the grade of tumor was concerned, well differentiated and poorly differentiated type of tumor was seen in 33.82% and 30% of cases respectively. (Table 4)

Main treatment modality used was External Radiation Therapy. Out of 680 patients, 248 (41.76%) completed the prescribed tumor dose of 60Gy, 16 patients received 50Gy; 244 patients received 40Gy and 136 patients, though started on radiation therapy, did not complete the initial dose of 40Gy. Adjuvant chemotherapy was given in 57 (0.67%) patients, after receiving the initial radiation therapy of 40Gy, (45 patients), and 60Gy (12 patients) of which 24 had adenocarcinoma and 33 squamous cell carcinoma. In most of these patients (40), tumor was located at esophagogastric junction. Surgery was performed only in 4 patients of esophagogastric junction with adenocarcinoma and followed by post operative radiotherapy of 40Gy (Table 5).

During treatment and subsequent follow-up, supraclavicular lymph node metastasis developed in 51, distant metastasis in 34, and tracheo-esophageal fistula in 16 patients. The predominant site of involvement with distant metastasis, were liver 14, lung 11, bone 7, brain 1 and skin 1. Among the bone metastasis, commonest sites of involvement were, dorsal spine in 5 and pelvic Bones in 2 patients. The length of follow up was measured from the day patients were started on radiotherapy treatment. The 1 year, 2 year, and 3 year survival rates were 15. 4, 10.0 and 4.4 percent respectively (Table 6)

DISCUSSION:

Cancer of the esophagus is an extremely common disease in India(4). It is the most common cancer seen in Kashmir and constitutes nearly 22.7% of all cancers. The incidence of squamous cell carcinoma is much higher (92.51%) followed by adenocarcinoma 7.35%. The incidence of esophageal carcinoma, especially adenocarcinoma, continues to increase by 5 - 10% per year in the US(9). We also observed an increase in the incidence of adenocarcinoma in the current study from 3.05% (1992) to 11.94%) (1995). The distribution of these two histologies has also changed dramatically across the years of this study, so far the location of the tumor is concerned. Adenocarcinoma in the middle esophagus (30cm) from incisor teeth and squamous cell carcinoma at esophagogastric junction (40cm from incisor teeth) was seen in 8 and 20 cases respectively. Majority (72%) of our patients had tumor located in the middle third of the esophagus, which is in accordance with that of other authors(3,4). The site of the lesion and the differentiation of the tumor does not have much prognostic significance. It is the histology and the stage of disease, which carries prognostic significance. Adenocarcinoma, irrespective of site has bad prognosis than squamous cell carcinoma. In the current study, 15 patients who were disease free, at the 4th year of follow-up had squamous cell carcinoma with well differentiated and poorly differentiated tumor in 9 and 6 cases respectively. This study demonstrated that radiotherapy and chemotherapy was the most frequently used regimen in the treatment of esophageal and esophagogastric junction carcinoma, 91% received radiation alone, 8% received radiation and chemotherapy while as less than 1% had undergone surgery followed by radiotherapy. Chemotherapy has been used as a treatment modality for esophageal carcinoma irrespective of stage or histology(10, 11). Also, radiation therapy alone has not been successful in the treatment of esophageal carcinoma, because of distant metastasis and local recurrence in more than 50% of cases(12, 13). During the period of current study, 51 patients, who were treated with radiation alone, developed nodal metastasis and 34 developed distant metastasis. This strongly justifies the role of chemotherapy. However, chemotherapeutic agents tried in this study did not prove beneficial in improving survival, though the number of these patients was small. Still more randomized trials need to be conducted in order to identify the more effective chemotherapeutic agents. The incidence of tracheoesophageal fistula, as reported by some investigators, is as high as 5-10% in patients with esophageal carcinoma(14).

The development of tracheo-esophageal fistula represents a grave prognostic sign. In our study tracheo-esophageal fistula developed in 16 cases (2.6%) and all of them died within 3 months after the development of fistula.

The optimal treatment of tracheoesophageal fistula resulting from locally aggressive esophageal cancer is still unknown(14). The overall survival rates in esophageal Carcinoma at 2, 3 and 4 years was 10%, 4.4% and 2.2% respectively. In the current study, though very poor, the results were not much different from other investigators, who reported 2 and 5 years survival rates in 8489 patients treated by external irradiation of 50Gy or more of 8 and 5% respectively(12-15). It is possible to identify the factors such as age and performance status that influence the ability to deliver full doses of radiation and chemotherapy(16). It is clear that little difference in over all survival occurs due to site or histology, whereas stage of the disease plays a major role in prognosis(9). In our study, a problem in selecting the patients for definitive treatment protocol was the inability to incorporate stage related factors such as tumor bulk that might have independent prognostic significance. Improved staging methods with the help of endoscopic ultrasonography were not performed because of its non-availability. Although, local control is frequently held to be the key quality- of- life issue in this disease, a prospective systematic evaluation of what constitutes adequate dysphagia free survival and the other factors that may have an impact on quality of life, need to be conducted.

Table 1
Patient Characteristics:

Age (Year)	Number of Patients N = 680	Percentage
<40 103	15.14	
41-50	291	42.79
51-60	216	31.76
61-70	030	04.41
>70	005	00.73
Unknown	035	05.14
Sex		
Male	390	57.36
Female	290	42.64

Table 2
Gross Lesion on Endoscopy :

Location of Tumor (cm)	Patient n = 680	Percentage
Ulcerative	167	24.55
Infiltrative	137	20.14
Polypoid	110	16.17
Proliferative	028	04.11
Strucuture	026	03.82
Nodular	014	02.05
Mixed	080	11.76
Unknown	018	02.64

Table 3
Endoscopic level of tumor location from incisor teeth :

Location of Tumor (cm)	Patient n = 680	Percentage
15-20	047	06.91
21-25	137	20.14
26-30	242	35.58
31-35	155	22.79
36-Esophagogastric junction	045	06.61
Esophagogastric junction	050	07.35
Unknown	004	00.58

Table 4
Histopathology & differentitation of Tumor:

Histology	Patients N = 680	Percentage
Squamous cell carcinoma	629	92.51
Adenocarcinoma	050	07.35
Oat cell type	001	00.14
Differentiation		
- Well differentiated	230	33.82
-Poorly differentiated	204	30.00
-Moderately differentiated	135	19.85
-Unknow	111	16.33

Table 5
Treatment Modalities:

Histology	Patients N = 680	Percentage
Radiotherapy alone	619	91.02
Radiotherapy plus Chemotherapy	057	08.38
Surgery plus Radiotherapy	004	00.58

Table 6
Follow-up:

Follow-up (months)	Lost*	Evaluable	Percent
<6	424	256	37.64
06-12	151	105	15.44
13-24	037	068	10.00
25-36	038	030	04.41
37-48	015	015	02.20

*Lost - considered dead.

CONCLUSION:

The overall prognosis of patients with esophageal cancer is very poor. It is hoped that the advent of intraluminal brachytherapy, conformal radiation therapy, careful surgery and judicious use of chemotherapy will help to bring the cure rate of cancer of esophagus close to that of other malignancies in general. The search for less toxic, more effective treatment modalities and the sequencing of therapies will have to continue. Further mass screening programmes in high risk population need to be conducted to detect the disease at its early stages to improve the survival.

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ABSTRACT

the hepatic microsomal cytochrome P450 3A4 isoenzyme and effects can, therefore, be potentiated by inhibitors of this enzyme including cannabis[5]. Other patients in whom the use of sildenfil citrate is potentially hazardous include those with active coronary ischemia, congestive heart failure or borderline low blood volume and low blood pressure status[3].

The patient reported by us was not on nitrates, had multiple risk factors (hypertension, dyslipidemia, smoking) and had consumed 100 mg of sildenafil citrate before engaging in sexual activity. Porter et al (1999) reported the case of a 65 years old man with known coronary artery disease who had an AMI shortly after taking sildenafil and engaging an sexual activity. The patient too had not been using nitrates[8].

It seems that the pharmacological effects of sildenafil add to the emotional arousal and physical stress of sexual activity and might precipitate acute plaque complications with superimposed coronary thrombosis. Further, although sildenafil is a relatively selective inhibitor of phosphodiesterase type 5, inhibition of this isozyme, which is present in platelets and vascular smooth muscle, as well as week inhibition of other isozymes presest in heart, could potentially cause adverse cardiovascular effects[3]. Since there is a small but finite increased risk of developing ischemia on sildenafil with sexual activity, the potential additional cardiac risk with the use of sildenafil citrate should always be discussed before prescribing the drug to patients with known cardiac disease or with multiple cardiovascular risk factors for ED irrespective of whether or not they are consuming nitrate preparations. Further, such patients should have a complete medical assessment that might also include an excercise stress test in appropriately selected patients[8].

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MALUNITED FRACTURE OF THE FIRST RIB WITH CONGENITAL FUSION OF ANTERIOR PART OF THE FIRST AND SECOND RIBS

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ABSTRACT

An unusual case of malunited fracture of the left first rib presenting as lump in the supra clavicular area of neck is reported for its rarity. The mechanism of injury in these cases is discussed and the literature on the subject is reviewed. This patient also had congenital fusion of the anterior parts of the first and second ribs on the left side.

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INTRODUCTION

Enlarged lymphnodes and various type of tumors are the commonest cause of lump at the supraclavicular area. Malunited fracture of the first rib presenting as lump at the supraclavicular region is an extremely rare condition.

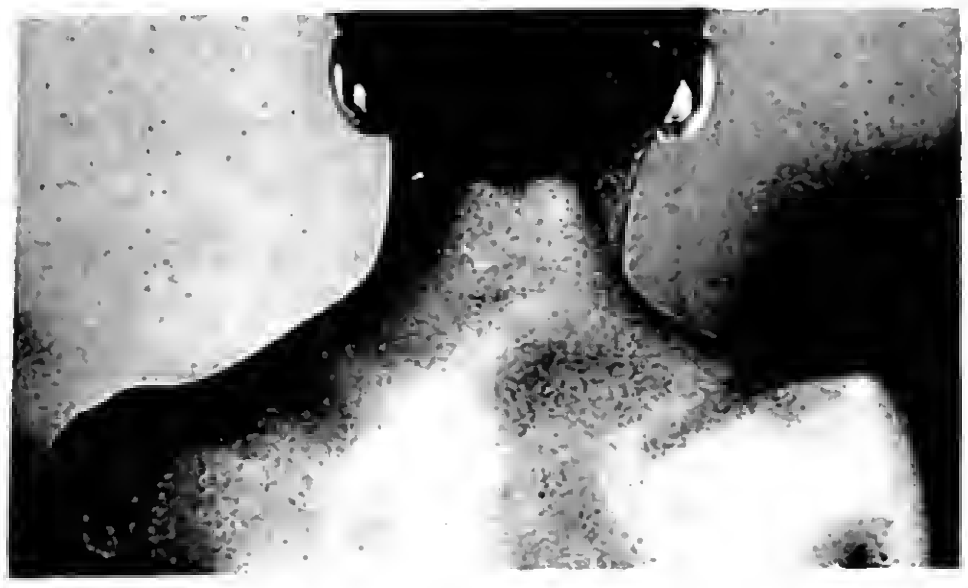

Fig. 1

Fracture of the first rib in itself is an uncommon injury[1]. In his review of 2014 cases of rib fractures, Liberson encountered only 3 cases of first rib fracture[2]. Congenital fusion of anterior parts of the first rib and second rib was also seen in our patient on the left side only. Therefore this becomes the first case of its kind in the literature. No such case has previously been reported to the best of our knowledge.

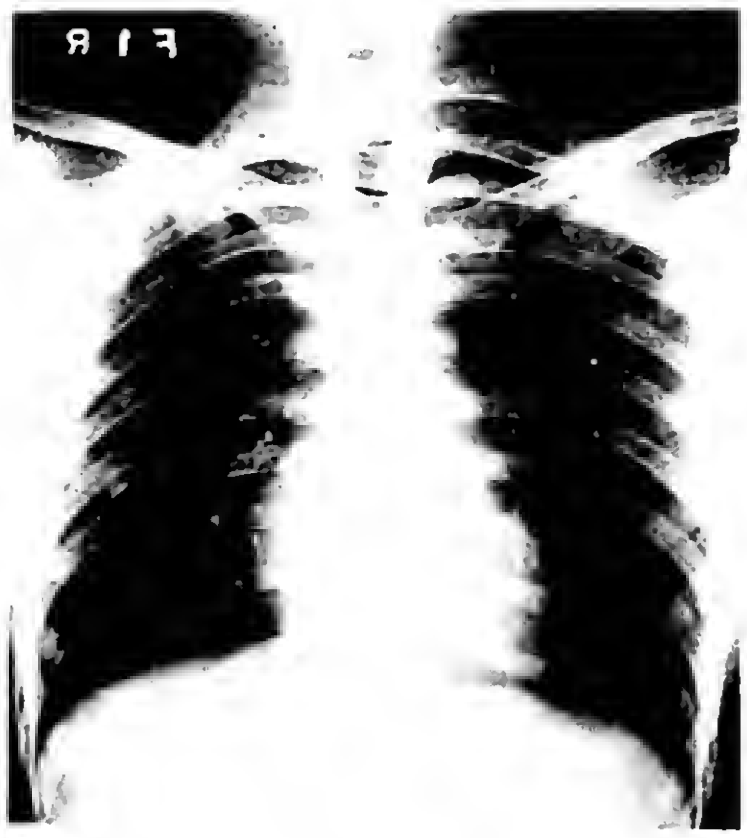

Fig. 2

CASE REPORT:

A 17 year old male patient came to our OPD with complaint of pain at his neck on carrying heavy loads for the last 25 days examination revealed a lump at the supraclavicualr region on left side of neck about an inch above the mid point of the clavicle. It was not mobile, irregular in shape and bony hard. It's size was about 1" X 1" and was not tender (Fig.1). There was no neurovascular deficit in the upper limb. He did not give any significant history of trauma. However the parents told that he fell down once from bed in early childhood around the age of 2 years. We were suspecting some bony tumor clinically. But the X-ray revealed an old fracture of the left first rib at the junction of posterior 1/3 and anterior 2/3 (Fig. 2). The anterior parts of the first and second ribs were fused on the left side (Congenital fusion). He was given rest and supportive treatment and recovery was uneventful.

DISCUSSION:

Fracture of the left first rib in a patient having congenital fusion of the anterior parts of the first two ribs on the left side is an extremely rare condition. No such case has previously been described in the literature to the best of our knowledge. Mechanism of injury to the first rib may be indirectly through the clavicle, directly from behind or in directly

Key words: Fracture, First Rib, Congenital fusion

through the manubrium. Later it was suggested that sudden and violent contractions of the scalenus mass can produce fracture of the first rib[3,4,5] Subsequently it was postulated that abnormal forces may pass across the clavicle through the subclavious muscle and costo-clavicular ligament to the costal cartilage and the anterior portion of the first rib[6].

Bilateral fractures are extremely rare only 24 cases have been reported till now[7,8,9] our case had pain in the supraclavicular region. Sudden hyperextension of the neck causing avulsion by scalene muscles can result in bilateral first rib fracture. Our case had only a unilateral fracture.

Unless There are complications like pneumothorax surgical emphysema or vascular injury, no special treatment is required. Reassurance, supportive measures and analgesics usually suffice. Most of these fractures can be expected to heal within 6 months although in some it may be delayed.

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CORRECTION OF POST OSTEOMYELITIC RADIAL CLUB HAND BY ILIZAROV TECHNIQUE

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ABSTRACT

The radius is a rare site of osteomyelites. Very less has been reported about the radial club hand resulting from osteomyelities. Different treatment modalities include bone grafting, centralization of wrist over distal ulna and radio ulnar transposition. Most of the treatment modalities aim at salvage only. This paper presents the use of Ilizarov technique of distraction followed by open radio ulnar transposition in an attempt to improve cosmesis and function of the hand.

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INTRODUCTION:

Radial club hand commonly presents as a congenital deformity, which arises as a result of the radial longitudinal deficiency resulting in radial hypoplasia, radial deviation of hand, pronation of hand, hypoplasia of thumb and ulnar hypoplasia. Similar presentation may occur from radial deficiencies due to osteomyelites. In western literature the incidence of ostoemyelites of radius has been quoted around 3 present[1]. In a retrospective study over 68 years Ono CM found post osteomyelitic radial club hand deformity in only nine patients[1]. In countries where osteomyelitis is still a common disease it is not uncommon to find such deofrmities with radial deficiency varying from small defect in radius to its total absence or leaving only the distal radial metaphysis carrying the carpus. The deformity left untreated, results in severe cosmetic and functional abnormality. Club hand resulting from osteomyelites has been reported less frequently[2,3,4,5]. Many methods exists for the centralization of such wrists but after the success in congenital cases, Ilizarov technique has shown promising results in terms of restoration of the hand function by increasing length of the forearm and better soft tissue management. While the literature is full of papers presenting the effectiveness of Ilizarov technique in the treatment of congenital cases[6,7,8,9], its use in the treatment of cases acquired as a result of osteomyelites has not been much described. This paper presents the correction of such deformity in two patients by Illizarov technique with good result.

REVIEW OF LITERATURE:

Different distraction apparatuses have been used differently to treat the congenital deformity. In one of the methods using Illizarov technique, distraction is achieved between two rings fixing the hand distally and the ulna proximally by separate rings connected by hinges and a distracting rod. Once the position of wrist is corrected, the forearm is either braced or the centralization is maintained by pin through wrist and bracing[10]. Kessler[11] recommends open centralization by creating a notch in the carpus to receive the ulna. Presently the preferred method has been using Ilizarov technique wherein an open release of the capsule at the distal end of ulna is performed through a dorsal incision[10]. The position of the wrist and hand is corrected by using distraction over a translational hinge. The procedure is followed by transposition of flexor carpi ulnaris to the dorso - ulnar side of the hand and the extensor carpi ulnaris is plicated. Ilizarov corrected the deformity by an extra articular ulnar osteotomy in which the distal ulnar segment is oriented as the corssbar of letter "T" on the shaft of distal ulna[10]. This procedure preserves the range of motion at the pseudo articulation and is best suited for adolescents or adults with neglected club hand, where this motion at the pseudo articulation is worth

Key words: Club Hand, Osteomyelites, Radius, Ilizarov technique

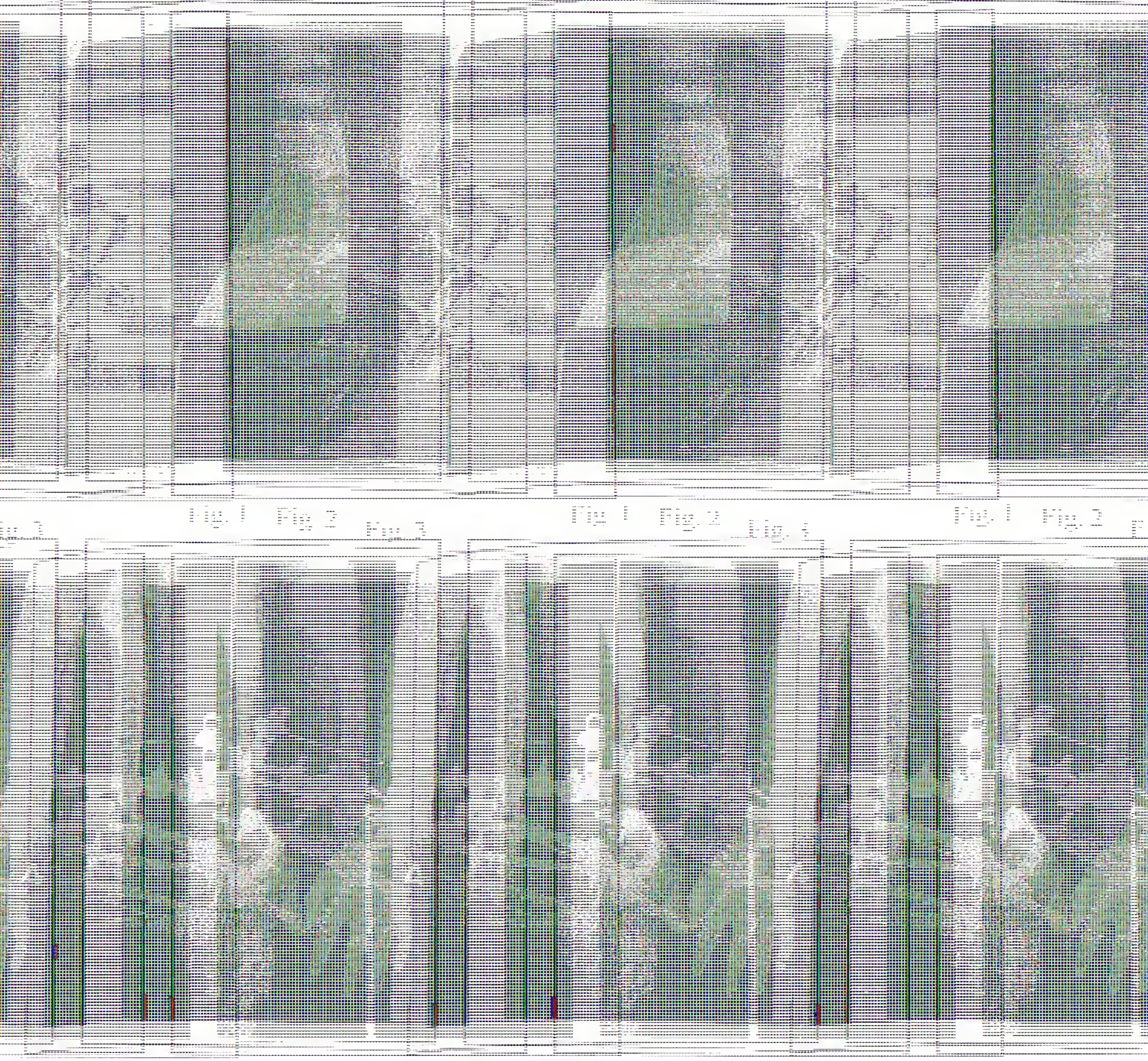

Fig. 1
Fig. 2
Fig. 3
Fig. 4
Fig. 5
Fig. 6

[illegible]

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two weeks. The total duration of treatment was 16 weeks. After removal of the cast patient was sent for regular physiotherapy. At the end of the treatment the goal of centralization of wrist, improvement of hand function, and realignment of the thumb was achieved without any soft tissue and skin problems (Fig. 4, 5 and 6). Patient was very happy with the improved appearance and function of his hand.

Case 2

14 years old girl had an attack of osteomyelites of radius at the age of 11 years. After multiple drainages and sequestrectomy the patient was left with deformed forearm. This patient presented to our OPD for correction of deformity. Examination revealed radial club hand on right side, with limited motion at wrist and the forearm fixed in pronation. Elbow movements ranged from 0-90 degrees. On radiography a major portion radius was found missing with distral ramnant of radius hypo plastic and tapering. Patient was also operated using Ilizarov technique. At the time of docking the forearm was fixed in functional postion. The ring fixator was removed after 11 weeks and a protective cast applied for 2 more weeks. After removal of the cast patient was advised to do physiotherapy. At the end of the treatment patient was happy with the result. During the treatment period the patient had mild pin tract infection, which resolved with antibiotics and dressing only.

DISCUSSION:

Different methods exist for the centralization of ulna in cases of congenital radial club hand. Acute correction requires special skin incisions and tendon and soft tissue lengthening. Gradual distraction using Ilizarov method provides many advantages like avoidance of special skin incisions. prevention of physeal damage and no need of tendon lengthenin. Ilizarov technique allows definitive treatment in such cases as it allows length equalization at the same time. The acquired club hand in adults is different in the sense that it does not have other associated skeletal and soft tissue defects other than radius and the ulna has a normal growth potential. In his review of nine cases Ono CM recommends that defects where where distal radius and the diaphysis are affected then centralization of the carpus over the distal ulna should be performed. Cases with intact distal metaphysis and small diaphyseal defects should be treated by bone grafting. Cases with large radial defect and intact distal epiphysis should be treated by radioulnar transposition. In our case we performed first distraction to overcome the soft tissue contracture followed by centralization at a second stage. There was no neurovascular problem or any difficulty with the union at radio ulnar transposition. In the case reported by Ono CM wherein ring fixation was used, the case needed bone grafting and ulnar osteotomy like our case, however, there was transient partial median nerve palsy during distraction period. The use of initial distraction is expected to better mange the soft to maintain the length of the tendons to put them in mechanical advantage. Disadvantage of this treatment is long treatment time and pin site problems Treatment in most of the patients of acquired radial club hand has improved cosmesis and the function has shown a varying degree of improvement and in may cases treatment is primarily considered as salvage only. Small number of such patients have been treated differently with the result it would be difficult to debate as to which method is the ideal one for treatment of such cases.

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Case Report

UNILATERAL MULTICYSTIC DYSPLASIA IN AN ADULT HORSE -SHOE KIDNEY - A CASE REPORT AND REVIEW OF LITERATURE.

Syed Sajjad Nazir, Baldev Singh Wazir, Shagufta Qazi

ABSTRACT

Horse-shoe kidney is the most common fusion anomaly of the kidney development affecting males twice than females and is vulnerable to diseases like infections, tumor, calculi, trauma and PUJ obstruction. Multicystic dysplasia occuring in a one or both segments of a horse-shoe kidney is a unusual occurence. Prognosis is best when the disease is unilateral. Nephrectomy is indicated if the dysplastic kidney is large enough to cause symptoms like G.I. or respiratory embarrassment, hypertension or malignancy. Only few cases have been reported in literature. We report here a case of unilateral multicystic dysplasia in an adult horse-show kidney.

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INTRODUCTION

Horse-shoe kidney is the most common fusion anomaly of kidney development and multicystic renal dysplasia represents a spectrum of pathologic states, from unilateral multicystic kidney through segmental and focal multicystic dysplasia to bilateral multicystic kidney.

CASE REPORT

A 22 year old male presented to us in January 2003 with history of fever, (L) flank mass and pain of 20 days duration. On examination patient was found grossly anemic, normotensive, febrile with temp of 1020F, with a mass in the left lumbar region extending towards the umblicus measuring about 10 x 15 cms oval, with irregular margins, ballotable, nontender and mobile. Rest of the clinical examination was normal.

Routine laboratory investigations revealed Hb 6.8 gm%, TLC 10,500, DLC N70L25E04M01. Blood and urine cultures were negative. Urine examination showed 10-15 cells. Ultrasonography reported - grossly hydronephrotic left kidney with normal low lying right kidney. CECT scan revealed horse shoe kidney with non-functioning multicystic component on left side with normal functioning right component and with no other abnormality. IVU showed non-visualization of left kidney with right kidney low lying, medially located renal pelvis with inferior convergence of the right lower pole with normally functioning right kidney. DTPA diuretic renal scan (F + 20 protocol) revealed non functioning left component of horse shoe kidney with normally functioning right component. VCUG was normal.

Pre-operatively three units of B+ve blood was transfused and patient was subjected to left nephrectomy. Operative findings revealed grossly enlarged left component of the horse shoe kidney composed almost entirely of cysts with very little stroma and occupying almost whole of the left abdomen. On cut section of the specimen, cysts were of various sizes and not communicating with each other. All components of the fluid within the cysts resembles plasma with respect to sodium, potassium, creatinine, urea and sugar, though protein was low than the plasma. Ureter was found partially obliterated with absent renal pelvis. Microscopic examination of the tissues situated between cysts revealed complete absence of normal renal architecture, an embryonic mesenchyma with primitive tubules and mal-developed glomeruli. The cysts were lined by low

Key words: horse-shoe kidney, multicystic, unilateral, dysplasia, nephrectomy, renal cyst.

cuboidal epithelium. Postoperative period was uneventful and patient is doing well at 3 months of follow up.

DISCUSSION

Horse shoe kidney is the most common fusion anomaly of kidney development[1]. The incidence is reported variously to be 1 of 353 cases[2], 1 of 400 cases[3], 1 of 425 cases[4] and 1 of 468 cases[5]. Males are affected twice as females. Multicystic dysplasia of horse shoe kidney is rare and only few cases have been reported[6] and can be unilateral or bilateral or one pole of a duplex kidney (Keneth), and in these instances, is associated with an atretic ureter and abnormal vasculature. The multicystic kidney represents a severe form of dysplasia and does not have a reniform configuration, and no calyceal drainage system in present. Typically, the kidney appears to be a "bunch of grapes" with little stroma between the cysts. The size of the cysts varies from slightly less than normal to enormous, filling most of the abdomen and contrary to stated conjecture[7], these cysts may communicate with one another.

In the view of Felson and Cussen[8], the multicystic kidney is an extreme form of hydronephrosis secondary to the atresia of the ureter or renal pelvis, which is a frequent concomitant condition. Hilderbrandt[9] suggested that failure of the union between the ureteric bud and the metanephric blastoma leads to cystic dilatation while Osathanondh and Potter[10], postulated that Potter type IIA kidneys, the type with large cysts, result from an ampullary abnormality in which the ampullae stop dividing early and therefore produce fewer generations of tubules.

The presenting symptoms of multicystic dysplastic kidney as stated by Spence[11], consists of a mass in the renal area in an otherwise healthy infant with non-function on the excretory urogram on the involved side in association with a normal contralateral kidney. In older children, multicystic renal dysplasia may be found incidently. Hypertension has been reported in several adult cases[6, 12]. The opposite kidney or other organ system are often abnormal6, an observation that was confirmed by Filmer and Taxy[13].

The diagnosis of MCDK, may occur after a radiologic investigation for a UTI, abdominal pain or an abdominal mass[14]. Imaging of the kidneys is indicated in certain conditions which are known to be associated with renal anomalies (eg. spina bifida, renal pancreatic hepatic dysplasia)[15-19]. In evaluating certain obstructive uropathies such as posterior urethral valves or ectopic ureter, the renal unit may be shown to be dysplastic. Sonogram helps to differentiate MCDK from UPJ obstruction[20].

In the light of the primitive nature of the nephron in a dysplastic kidney it is not surprising to note that these kidneys have little to no function on studies such as a renal scan[20], utilizing either Tc99m DMSA/MAG^3 or DTPA Tc99m or IVU[14]. The kidney, however, may have limited function due to some residual normal glomeruli and rarely represents more than 5% of total renal function when present[21]. Other modalities that may be of use in localizing the dysplastic kidney is CT scan or MRI[22].

The ultimate question regarding the dysplastic kidney is whether it needs to be removed or not. Clearly if the dysplastic kidney is large enough to cause gastrointestinal or respiratory embarrassment it should be removed expeditiously and is seen occasionally in the multiple variety of dysplasia.

The longest clinical experience with MCDK, is the multicystic dysplastic kidney registry of the American Academy of Pediatrics section on Urology[23]. Their 441 patients were registered from nearly 50 hospitals in North America. Nephrectomies were performed in 181 patients and 260 patients were managed conservatively. The natural history of these MCKDs with regards to involution was based solely on sonographic findings. Of the MCDKs followed for 1-3 years, 47% decreased in size, 37% remained the same size and 13% disappeared. At 3 to 5 years 23% had disappeared. A greater rate of resolution was seen by Orejas et al; in their series, 75% of the MCDKs involuted[24].

In the MCDK registry, no patients required nephrectomy due to infection. The registry has reported no cases of hypertension attributable to the MCDK. There were only 6 cases of tumour formation; 3 were in adults and 3 were in the pediatric age group. Based on the low incidence of infections, hypertension and tumours, the registry suggests that it is reasonable to manage these patients non-operatively and obtain sonograms every 3 to 6 months in the first year of life, every 6 to 12 months in the next four years and possibly yearly thereafter. Others[25-26, 28, 29] recommended that nephrectomy not be performed in the asymptomatic child with a MCDK.

CONCLUSION

Horse shoe kidney is the most common fusion anomaly of the kidney and is vulnerable to diseases like infections, tumours, calculi and PUJ obstruction, in the same way as normal kidney. Multicystic dysplasia occurring in a one or both segments of a horse shoe kidney is an unusual occurrence and is a grave disease. Prognosis is best when the disease is unilateral, the contralateral kidney is normal and other major anomalies are absent. Careful assessment of the opposite kidney is vital before establishing a prognosis. Bilateral disease is incompatible with life. Diagnosis is usually made by sonogram, renal scan and CT/IVU/MRI. Nephrectomy is performed when there is gastrointestinal or respiratory embarassement, infection, hypertension or tumour formation. Involution also occurs and long term follow up is necessary for patients managed conservatively.

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MULTIPLE EVANESCENT WHITE DOT SYNDROME

Sabia Rashid, M.S., Junaid.S. Wani, M.S., A.R.Nasti, M.S.

ABSTRACT

A young female presenting with blurring of vision and photopsia was diagnosed as a case of Multiple evanescent white dot syndrome(MEWDS) on fundus fluorescein angiography(FFA).This case is being reported considering the rarity of the disease and also to emphasize its benign and self limiting course which requires no treatment.Moreover it is commonly mistaken and has to be differentiated from papillitis which needs more aggressive treatment.

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INTRODUCTION

Multiple evanescent white dot syndrome(MEWDS) is a rare,benign, acute,self limiting disorder which usually affects young females.It is mostly unilateral.Very rarely this disorder can be bilateral.There is usually a significant visual loss early on but returns to normal within 4 to 6 weeks.Recurrences have also been reported in a few patients.[1-8]

It is an inflammatory disorder of unknown etiology and results in acute visual loss or photopsia.It primarily involves the retinal pigment epithelium and photoreceptors but the lesions can extend into the choriod as well.Retinal lesions are transient and include white dots,optic nerve head swelling,enlarged blind spot,paracentral and central scotomas.[1,9,10]

The timing of examination is crucial for accurate diagnosis because the retinal lesions are transient.[9]

No active treatment is required and visual prognosis remains good for unilateral,bilateral as well as recurrent forms of the disease.

CASE REPORT:

A 30 year old female reported to the Eye OPD of SMHS Hospital with chief complaints of blurring of vision and photopsia of one week's duration.There was no history of any preceeding illness or constitutional symptoms.General physical examination did not reveal any evidence of systemic disease.Complete blood count and ESR was within normal limits.Fasting blood sugar was 79mg/dl.Antinuclear antibody was negative and serum immunoglobins were within normal range.

The visual acuity in the right eye was 6/9 and that in the left eye was 6/36.Anterior segment of both eyes was normal and both pupils were reacting briskly to direct and consensual light.Vitreous cells were seen in the left eye.Fundus examination of right eye was normal but the left eye showed disc hyperemia and blurring of the margins.Nerve fiber layer showed hemorrhage superior to the disc and white dots which were seen mostly in the paramacular area. Macula showed granular white dots.

Fundus fluorescein angiography (FFA) in the right eye showed a few areas of hyperfluorescence along the inferotemporal arcade in the mid and late phase without disc leakage.FFA of the left eye showed areas of blocked fluorescence in the early phase with diffuse and patchy hyperfluorescence of these spots in the mid and late phase associated with early disc leakage. (Fig: 1a&b)

The patient was put on ketorolac eye drops and was examined four weeks later.There was a marked improvement in visual symptoms.Visual acuity repeated after four weeks was 6/9 in the right eye and 6/12 in the left eye.FFA was again performed after six weeks and was normal in the right eye. FFA of the left eye revealed no disc leakage and very few hyperfluorescent spots.(Fig: 2 a&b)

DISCUSSION:

MEWDS has been described as a rare,acute,self limiting disease of unknown etiology which usually affects young females.

Most of the cases reported so far have been unilateral with a good visual

Key words: Multiple evanescent white dot syndrome (MEWDS),Fundus fluorescein angiography (FFA).

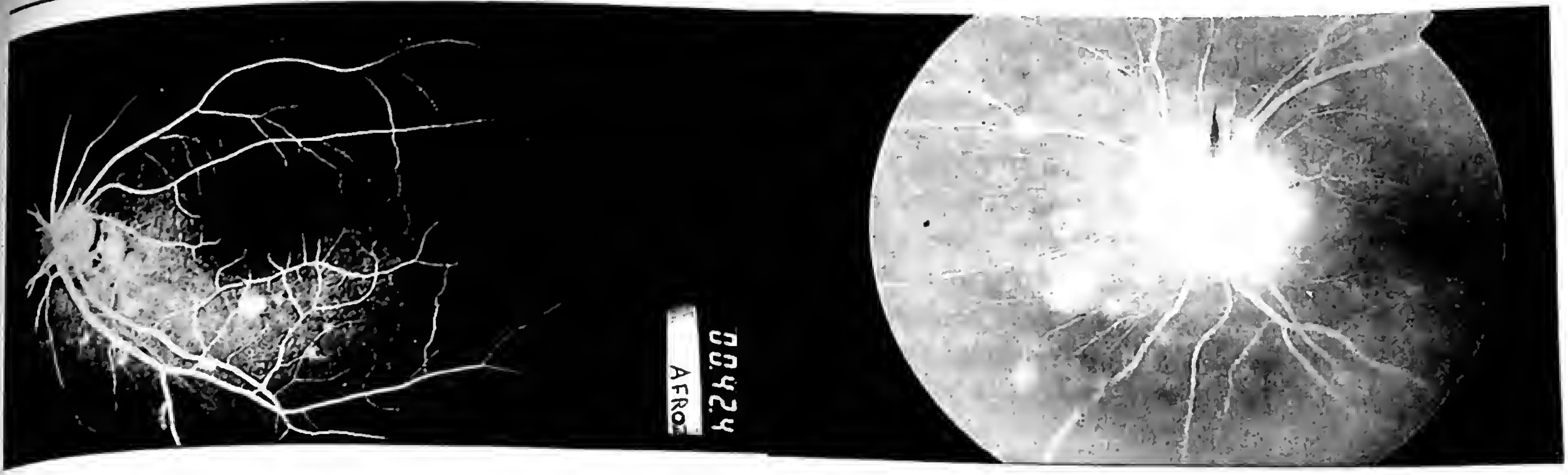

Fig. 1 (a & b)

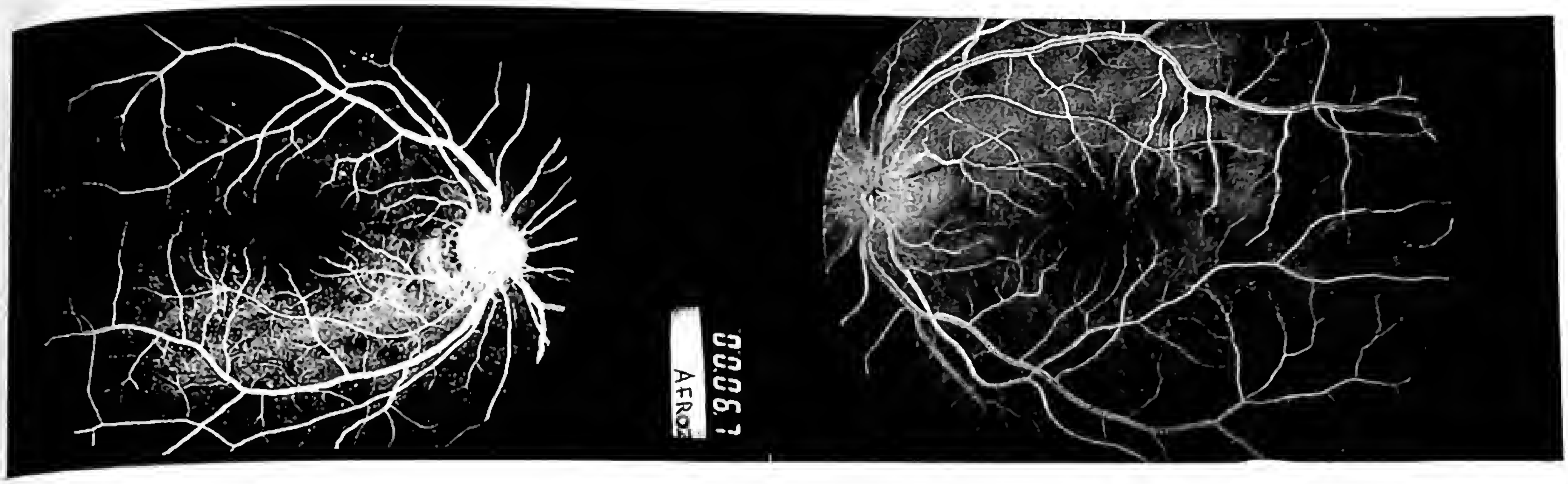

Fig. 2 (a & b)

outcome. However bilateral involvement,though rare, is also known and carries an equally good visual prognosis as shown in anecdotal reports.Patients with bilateral disease are known to exhibit asymmetrical distribution pattern on FFA.Our patient also had bilateral disease, one eye affected more than the other and showed satisfactory subjective and objective improvement within six weeks conforming to previous reports.[3-8]

It has been shown that retinal angiographic findings exhibit much more extensive disease than is indicated by the functional examination.[9] This observation holds true for our patient as well who had minimal diminution of vision in the right eye but the FFA was abnormal.

The timing of examination is crucial for diagnosis because the retinal findings are transient and evanescent,thus distinguishing it from other inflammatory disorders like papillitis which require more aggressive treatment.[10]

There are a few reports of recurrences of MEWDS which can occur months to years after the first attack.The visual prognosis in the recurrent form of the disease is also good.Our patient showed complete recovery and is on follow-up for any future events.

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CRYPTOCOCCAL MENINGITIS IN A PATIENT ON STEROIDS

Tehmeena Wani M.D, Dalip Kumar Kakru M.D, Mushtaq Ahmed Wani, Manzoor Ahmad Thokar, Bashir Ahmed Fomda, Gulnaz BashirM.D

ABSTRACT

A 43 year old woman with a provisional diagnosis of Tuberculous meningitis, Septicemia and Encephalopathy was admitted on neurology side at Sheri- Kashmir institute of medical Sciences, Srinagar. Cryptococcus neoformans var. gatti was isolated.

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INTRODUCTION:

Cryptococcosis is a chronic subacute or rarely acute pulmonary, systemic or meningeal infection caused by the yeast C.neoformans. The incidence of cryptococcosis has increased in many areas corresponding with the pandemic of AIDS, being a major cause of morbidity and mortality among patients with AIDS. Cryptococcosis also occurs in people with other cell mediated immune defects such as lymphomas, chronic leukemias, organ transplantation and those receiving steroids[1]. In India though isolated cases of cryptococcosis have been reported from different centres[2], incidence of cryptococcosis in Kashmir has been rare. A case of cryptococcal meningitis which we are reporting from Kashmir is only the second case being reported after a gap of sixteen years ,the first case of cryptococcal meningitis having been reported in a non- AIDS patient from our hospital in 1987[3].

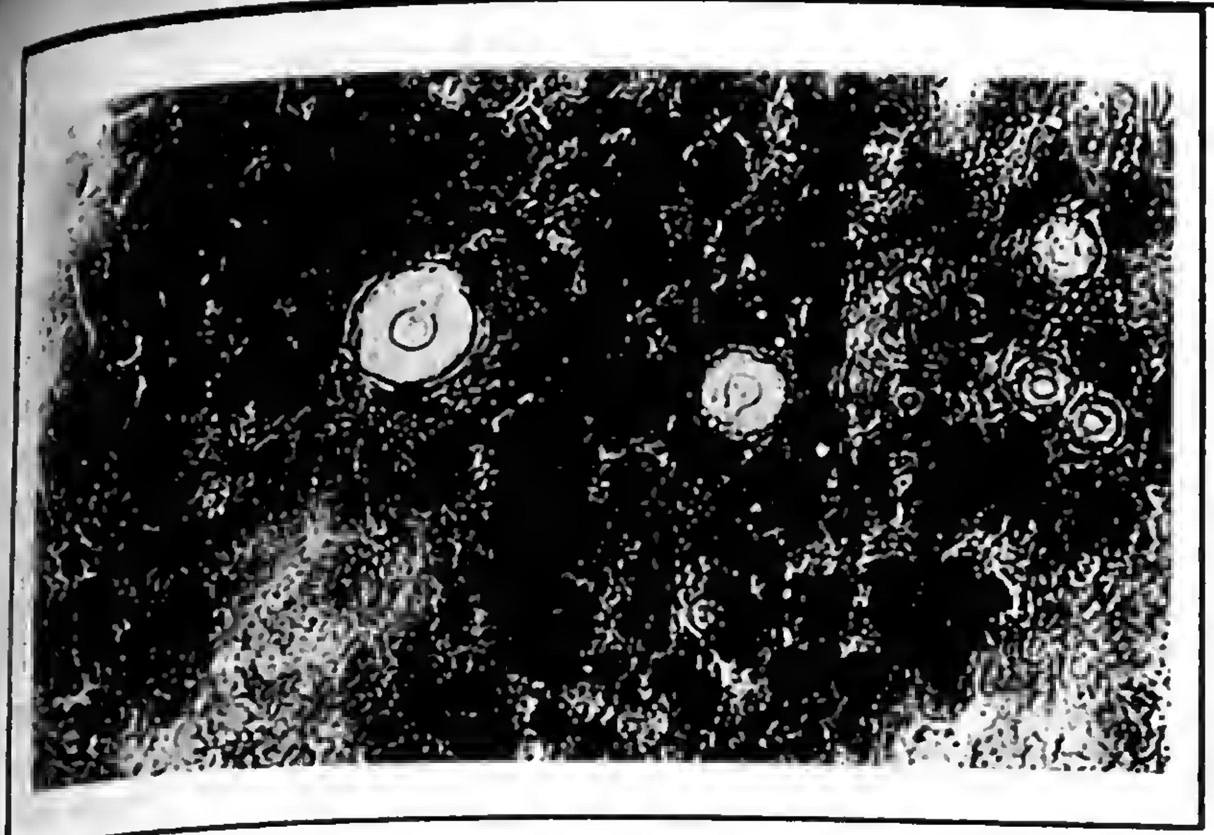
CASE REPORT:

A 43 year old woman with a provisional diagnosis of tuberculous meningitis, septicemia and encephalopathy was admitted in neurology ward of SKIMS with complaints of headache, impaired memory, judgement and fever (38.5° C) of one month duration. Past history revealed that the patient had pulmonary kochs in 1990 for which she was treated with anti-tubercular drugs. Patient also was a case of Rheumatoid arthritis, receiving Wysolone 10mg per day for the last ten years.CSF obtained by lumbar puncture was received in the department of Microbiology . Wet mount Gram staining and India ink preparation revealed 3-7 um round budding yeasts with a capsule. CSF was cultured by standard procedures[4]. Creamy white mucoid colonies appeared on Sabouraud dextrose agar after 48 hrs.The identification and pathogenicity of Cryptococcus neoformans was established by growth at 37°C,urease production and mouse pathogenicity test.Serotyping of the isolate showed it to be C.neoformans Var.gatti.Incidently, AFB smear and culture of CSF were negative.Neurology department was informed and the diagnosis was revised.Patient died before they could get a chance to put her on anti-fungal therapy.

DISCUSSION:

C.neoformans is an encapsulated yeast like fungus that reproduces by budding and is ubiquitous in soil and avian guano.Antigenic specificity of the capsular polysaccharide defines four different serotypes of C.neoformans --- A,B,C and D. Serotypes A and D are classified as C . neoformans var.neoformans and serotypes B and C are classified as C.neoformans var.gatti[5] C.neoformans var.neoformans has a world wide distribution and can infect both immunocompetent and immunodeficient subjects. C. neoformans var.gatti, which has been isolated in the present case is found as a mycelium on Eucalyptus camaldulensis tree. This type is less commonly seen in AIDS patients but is reported to cause severe pneumonia

Key words: Cryptococcus, Meningitis, Steroids



Photomicrograph showing budding yeast cells with large capsule the mouse brain tissue (India - ink preparation 400x)

and meningitis in immunocompetent patients[6].
The reason for the predilection of Cryptococcus for the CNS has not been explained. The organism probably encounters less cellular(phagocytic)response there, and it has been theorized that selective nutritional factors for the yeasts are present. Simple sources of nitrogen, such as asparagine and creatinine are found in the spinal fluid[4].
Corticosteroids have varying types and degrees of effect on cellular immune function and in conjunction with the status of the underlying disease, interact to predispose to specific infections. Patients with immunologic defects in T-cell mediated host defence mechanism appear to be at increased risk for progressive cryptococcosis. High dose corticosteroid therapy is an important and frequent risk factor for cryptococcosis, even therapeutic doses of corticosteroids predisposed to cryptococcal infections[7]. Microbiological diagnosis is useful for prognostic reasons and may save patient's unnecessary treatment if tuberculous meningitis is the alternative diagnosis[8]. Immunosupression through the use of corticosteroids should be noted and alert the clinician to the possible presence of an unusual pathogen. Patients who have been treated with a steroid are more likely to have Cryptococcal or tuberculous meningitis[9].

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SERRATIA MARCESCENS PNEUMONIA

Zuhra Jabeen, Rukhsana Asif, Kadri SM, Basharat Alam, Shaw Tabasum

Serratia marcescens is an aerobic gram-negative bacillus belonging to the family Enterobacteriaceae. It is an opportunistic organism easily transmitted by hands and can produce septicemia, endocarditis, meningitis and wound and urinary tract infections. It is an uncommon cause of peneumonia and commonly occurs in individuals with underlying cardiopulmonary disease and immunosuppression. We report the occurrence of this penumonia in an elderly individual with underlying chronic obstructive lung disease. To our knowledge, this is the first case reported from India so far.

A 60 - year- old male of chronic obstructive lung disease was admitted to the Department of Internal Medicine, SMHS Hospital, Government Medical College, Srinagar, Kashmir, India with history of fever of 6 weeks duration followed by anorexia and productive cough. On examination, he was plethoric, cyanosed with coarse rales and wheeze on both sides of chest and signs of consolidation in the right lower lobe. Other systemic examination was normal.

On investigating his hemoglobin was 7g/dl, total leukocyte count of 7.6x 10^3/micro liter with 63.4% neutrophils. Chest radiograph revealed consolidation on right lower zone and prominent bronchovascular markings on both sides. Sputum was taken for culture and sensitivity using Mac conkey's agar, Blood agar and nutrient agar. On Mac conkey's agar colonies were convex, circular colonies and red in color 1-2mm in diameter greater than 10^4 CFU/ml and several sputa were cultured and the organism was isolated more than three times. Gram staining of colonies showed gram-negative bacilli. The biochemical profile was Indole-negative, Methyl red-negative, VP-positive, Simmons citrate-positive, Lysine decarboxylase-positive, lactose fermentation-negative, Urease-negative, H2S-negative, PPA-negative, Motility-positive, Glucose fermented with gas production. Sucrose and Mannitol fermented. Organism sensitive to Amikacin, Sparfloxocin, Ciprofloxacin, Ceftazidime, Ceftriazone resistant to Cephalexin, Tetracycline, Cephadroxil and Amoxycillin. Urine and blood cultures were sterile. The patient was put on Amikacin and he showed clinical and radiological improvement with in a week of therapy.

Serratia marcescens is an uncommon gram-negative aerobic motile organism known to cause speticemia, endocarditis, meningitis, wound infections and urinary tract infections. Pneumonia as was noticed in our patient is less common and usually occurs in elderly individuals with underlying cardiopulmonary disease and the use of contaminated respiratory therapy equipment[1,3]. However, Khan EA et al[2] reported pneumonia, empyaema and pneumatocele formation due to this organism in a neonate. The clinical features of Serratia marcescens penumonia include fever, chills and productive cough; pseodohemoptysis may be one of the presenting features because of the pigment, prodiagiosin produced by the ogranisms[1]. Mild leucocytosis is usual although it was not noticeable in our case. Mortality with this pneumonia may be as high as 80%[1], other strains of Serratia include Serratia plymuthica, Serratia liquefaciens, Serratia rubidaea and Serratia odorifera and among all the strains, Serratia marcescens is known to cause disease[4].

In the hospital Serratia tends to colonise to the respiratory and urinary tracts and only since 1960 Serratia marcescens has been recognized as an opportunities human pathogen, other illness related to this organism include keratitis, endophthalmitis, cellulites, phlelutis, otitis media and parotitis [3,4,5], however, such an illness was not found in our case.

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METASTASIS OF CARCINOMA CERVIX

A patient was admitted with history of continuous bleeding pervagina 10 days. Her obstetric history Para 4 all full term normal deliveries, not ligated. On exam general condition was good. P/A soft P/V cervix was hypertrophied, bled on touch. Pt was investigated for cervical Biopsy and Examination under anaesthesia.

On perspeculum examination Cervix was hypertrophied, eaten up. irregular, friable and bled on touch cervical biopsy was taken at 2 sites (1) from friable area and (2) healthy area.

On pervaginum examination Fornices were free with no Parametrium involvement. Rectum was free. Endometrial curretings were scanty and also taken for HPE.

HPE. Showed proliferative phase endometrium with fragments of squamous cells and acute endometritis. Cervix showed ulcerative growth, replacing of cervix with transmural infiltration.

Operation - Pan hystrectomy performed on 24th August 2001.

Vaginal cuff was removed with involvement shown on posterior and left side. Vaginal cuff was removed well beyond infiltrated zone. Ureters were found well beyond the infiltration area.

Histopathological report of Specimens.

A. Uterus: 40mm x 40mm x 30mm lower end of endometrium and myometrium were infiltrated.

B. Ovaries: Left ovary 20mm x 20mm x 10mm
Right ovary 30mm x 25mm x 20mm
Fallopian tubes were free.

C. Cervix: 28mm x 25mm shows ulcerating growth, replacing of cervix with transmural infiltration. Mixed squamous cell carcinoma and adenocarcinoma (collision tumour) cervix, with Transmural infiltration.

D. Vaginal Cuff: Was infiltrated.

Inference Carcinoma cervix stage Ia.

- Pan hysterectomy c Removal of vaginal cuff.
- Internal Iliac node was removed.
- Paraaortic nodes not involved.

Following surgery Pt sent to Soura for Radiotherapy.

The patient was admitted exactly one year later on 28-8-2002 at SKIMS hospital Bemina with a different complaint of pain in paraumblical region. An orange sized mass hard and tender felt in the region on per abdomenal examination. Ultrasound showed a mixed echogenic mass on rectus muscle underneath the skin. FANC done was not conclusive. Skin over the swelling not involved.

Exploration of this parietal wall swelling was done at SKIMS hospital Bemina on 10-9-2002. Midline incision over the swelling area was given. Immediately under the Skin, a stony hard fixed Mass addherent to the parietal wall. the rectus shealth and muscle was noticed. No connection with peritoneal cavity Mass excised by sharp dissection along with some healthy margin of tissue. Umblicus excised for fear of developing umblical fistula. Liver Bowel, omentum, diaphragm, appendix felt all were normal. No pelvic nodes were felt.

Drain kept - one in parietal wall and one in peritoneal cavity.

This mass in the parietal wall proved secondary to carcinoma of cervix, arising from the squamous cells of the skin.

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HYDATID CYST OF LIVER-A LAPAROSCOPIC MANAGEMENT

Hydatid cyst is a parasitic disaease caused by Echinococcus granulosus known as classic hydatid disease.Echinococcus multilocularis results in alveolar hydatid disease, a less localised disease and both are continuing public health problem in state of Jammu and kashmir where sheep herding and breeding is a widespread profession.We present a case report of hydatid disease of liver managed laparoscopically with good results.

A 32 year male was admitted in our hospital with pain right hypochondrium since 6 months. Ultrasound showed echogenic mass of 9x9 cm with multiple daughter cysts and clear fluid.Computerized Tomography showed a well defined hypodense lesion of 9x9 cm at right lobe of liver with multiple areas of increased densities with no calcifications. Preoperatively patient was put on albendazole10mg/kg/day for 10 days..Patient was posted for surgery and laparoscopic cystectomy was planned.Patient was put in supine position with head raised and left lateral tilt . A specially designed port [12mm] having 15inches length with a long sheath which reaches into deep seated cavity was used. It has a side channel of same diameter through which a strong suction was done and entire contents of cyst were evacuated. Patient recovered well postoperatively and had no recurrence of symptoms over a follow up of one year.

Echinococcus is present in the intestine of carnivore like dog which is the definitive host. Eggs are ingested by herbivore like sheep which is intermediate host and goes to liver through portal vein where it forms hydatid cyst. Man is an accidental host. Most common sites are liver (60%) and lung(30%). Pain in right upper abdomen is the most common symptom. Specificity of ultrasound is 90% and CT scan is 100%. Modes of management have been medical with mebendazole and albendazole.

Surgery for hydatid cyst of liver are percutaneous aspiration, marsupilization, partial or total pericystectomy and liver resections. Akin et al concluded in his study that surgical management of hydatid disease without drainage decreases postoperative complication rate and average hospitalization period[1]

Demirbilk et al studied and compared the results of medical treatment and various surgical treatment between 1988 to 1997 and concluded that surgical treatment offers early cure than medical treatment.[2]

Laparoscopic surgery has added new dimension to hydatid cyst surgery. Patients with small size and early stage cysts are ideal cases for laparoscopic treatment as wall collapses after laparoscopic evacuation.

Ertem et al studied 12 patients of hydatid cyst of liver and treated them laparoscopically and concluded that these patients had postoperative comfort, less pain, better scar, decreased hospital stay and early return to daily activities.[3]

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CLINICAL APPLICATIONS OF ANTIPHOSPHOLIPID ANTIBODIES - AN OVERVIEW

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The detection of antiphospholipid antibodies (aPL) namely - lupus anticoagulant (LA) or anticardiolipin antibodies (aCL) is of considerable interest because of their importance in the pathogenesis of clotting in the antiphospholipid syndrome (APS) a condition present not only in the autoimmune diseases but also in patients who do not manifest any overt symptoms of autoimmune disturbance (primary APS) where the emphasis is primarily on vascular events(1,2).

The antiphospholipid antibodies were first detected by Wasserman(3). In 1983, at the Hammersmith Hospital cardiolipin was used for the first time as the antigen in solid phase antiphospholipid specific assays by Harris et al(4) and the term APS was born(5). These are a diverse family of autoantibodies which share in common a reactivity with negatively charged phospholipids. Cardiolipin is a double negatively charged phospholipid held together by the glycerol linkage. It reacts with a lipid hapten of bovine heart and hence the name cardiolipin. Antibodies to phospholipid antigens such as cardiolipin play a crucial role in coagulation abnormalities(6). Those responsible for this anticoagulant activity bind various negatively charged phospholipids including cardiolipin(7). These antibodies in vitro prolong coagulation whereas in vivo they promote thrombosis.

These antiphospholipids belong to a heterogeneous family of antibodies diagnosed either by clotting tests: the lupus anticoagulants or by ELISA: anticardiolipin (aCL) and anti-beta 2 glycoprotein (anti-beta2 GPI) especially. The heterogeneity of aPLS makes a comprehensive approach to laboratory investigations essential. Detection of lupus anticoagulant relies on increased clotting times in phospholipid dependent tests. Their 4 step diagnosis includes: 1) Screening (by at least two different tests); 2) demonstration of an inhibitory activity; 3) evidence of its phospholipid dependence; 4) exclusion of an associated coagulopathy. Among the aPLS detected by ELISA, IgG aCL are the most frequently investigated. However, other antibodies may represent useful biological trials. Among them, anti-beta 2 GP1 are thought to be more closely associated with a history of thrombosis than aCL and testing for anti-beta 2 GP1 should now be systematically included in the biological diagnosis of APS(8).

Antiphospholipid antibodies are found in:

i) 30-80% of SLE. The presence of APA in SLE patients is associated with an increased risk of thrombosis, thrombocytopenia, haemolytic anemia, stroke, chorea transverse myelitis, hypertension and livedo reticularis(9).

ii) Patients taking drugs like cocaine, interferon, hydralazine, phenothiazine, quinidine, phenytoin.

iii) Chronic infections like syphilis, infectious mononucleosis(10), tuberculosis, leprosy (11), leptospirosis, malaria, typhus, palsies, CMV infection(12), hepatitis C(13) and HIV infection(14,15).

iv) Primary antiphospholipid antibody syndrome (Hughes syndrome).

There are two hypothesis for the mechanism of action of anticardiolipin antibodies. The first one is that antibodies might damage platelet membrane leading to subtle changes in platelet functions(16). The second states an effect on endothelial membranes leading to decreased prostacyclin release(17). These antibodies have been linked to adverse pregnancy events. Pregnant woman possessing these antibodies have an increased risk of spontaneous abortions, still births, intrauterine fetal growth retardation, preterm birth and arterial and venous thrombosis. Antiphospholipid antibodies may decrease or disappear between pregnancies only to recur with increased activity in subsequent pregnancy and lead to fetal loss. It has been suggested that women with a history of recurrent abortion or fetal death could benefit from screening for circulating antiphospholipid antibodies.

Prior foetal loss is a powerful independent predictor of future foetal loss as foetal death is increased in women with high titres of IgG aCL and lupus anticoagulant. Decrease in titres of a anticardiolipin during pregnancy does not confer protection for that pregnancy. Therefore, normalization of lupus anticoagulant or anticardiolipin titres should not be used as an end point for treatment.

Foetal well being should be assessed by monitoring heart rate, biophysical profile and umbilical artery doppler waveforms(18).

Antiphospholipid syndrome though initially seen as small print syndrome is now known to be common, important and potentially treatable. The syndrome is described as a cross-road to autoimmunity and atherosclerosis. It is characterized by arterial and venous thrombosis either primary or secondary to connective tissue disease and malignancy. Cardinal features of antiphospholipid syndrome (APS) are (a) recurrent thromboembolism (b) recurrent foetal loss (c) livido reticularis. Other common features are thromboembolism, non-stroke haematological events, valvular heart disease and catastrophic vascular occlusion. There are two types of APS. Primary APS without associated collagen vascular disease like SLE and sustained high titre of IgG aCL > 40. Secondary APS with associated collagen vascular disease like SLE and transient high titres of IgG anticardiolipin and transient or sustained high tires > 40 of IgM or IgA anticardiolipin. Proposed mechanisms of thrombosis are:-

I Antibody interference with haemostatic reactions on the membrane surface.

II Autoantibody engagement of antigen on cell surface leading to transduction of signal and altered cell activity.

III In vivo interference with physiological anticoagulant reactions such as those with protein C and protein S pathway may have a procoagulant affect.

IV Autoantibodies binding to beta 2 glycoprotein I on endothelial surface induce expression of adhesion molecules: E selectin, VACAM 1, ICAM1 and enhance monocyte adhesion to endothelial cells(19,20).

APS may account for 15-20% of all episodes of DVT, one third of all episodes of strokes occuring in patients below the age of 50 and 5-15% of females with recurrent foetal loss.

Classification of APS syndrome:

Type 1: DVT with pulmonary thromboembolism.
Type 2: Coronary or peripheral artery thrombosis
Type 3: Cerebrovascular or retinal artery thrombosis
Type 4: Mixed

Clinically the effects of thrombosis on brain are major and profound since brain is rich in phospholipids. Hence there is direct effect on neuron(21), arterial occlusion is the most common event in APS. In small vessel brain disease, endothelial hyperplasia of meningeal and cortical arteries suggests that local vascular injury as preceded thrombosis. Vessels of any size may be affected after the first stroke, the risk of recurrent stroke is approximate 20% per year and 60% overall.

Catastrophic antiphospholipid syndrome:

This unusual and potentially fatal subset of the APS was first defined in 1992(22) since then, more than 150 patients have been reported(23). Triggering factors have become apparent and these have included trauma, withdrawal of anticoagulation, carcinoma and also infections(24). The latest analysis has shown that 35% of cases of catastrophic APS were preceded by infections. These comprised respiratory (15%), cutaneous (8%), urinary tract (6%), gastrointestinal (1%), general sepsis (1%) and others (9%)(25,26). This syndrome is often fatal characterized by multiple organ infarction over a period of days to weeks. It is seen in antiphospholipid positive patients who have borderline levels of antiphospholipid and borderline platelet count and suddenly there is severe thrombocytopenia, adult respiratory distress syndrome, coma and multiorgan failure and in most cases death(27).

In conclusion the identification of the syndrome is clinically important because of the risk of recurrent thrombosis and the need for antithrombotic therapy in many cases(28). There is a need to study the different possible antigens of antiphospholipid antibodies as well as their specificities and pathological mechanisms in greater depth in order to obtain a phospholipid immunity marker that is useful in the diagnosis of these positive patients.

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CURRENT PRACTICES OF BIO-MEDICAL WASTE MANAGEMENT IN GOVERNMENT MEDICAL COLLEGE ASSOCIATED S.M.H.S.HOSPITAL, SRINAGAR, J&K, INDIA

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ABSTRACT

To assess Current practices of Bio-Medical Waste management including production, collection, transportation, storage, treatment and disposal technologies, and planning of Bio-Medical Waste Management and infection control in S.M.H.S. Hospital Srinagar; and to assess health and safety practices for healtcare personnel in Government Medical College Associated S.M.H.S. Hospital, Srinagar an observational study using interview method was conducted in S.M.H.S. Hospital, an associated hospital of Government Medical College, Srinagar. Around 750 bedded, S.M.H.S. Hospital, an associated hospital of Government Medical College, Srinagar is the second biggest hospital in the valley with annual OPD influx of more than 12 lac patients and about 4,200 inpatients admitted annually. Each in-patient patient generates about 2 kg of waste generated per annum is approximately 650 tonnes. Every day the BMW is collected by in-service sanitation staff-collecting, carrying in plastic in waste-dumper of Municipality. The BMW generated is not segregated and is either burnt in incinerator or lifted by SMC for open dumping (or land filling), thus not fulfilling the requirements envisaged in Bio-Medical Wastes (management and Handling) Rules 1998.

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INTRODUCTION

During last few decades, the need for better health-care has been felt globally and Kashmir is no exception to it. To cater to the needs and demands of the increasing population, a rapid mushrooming of hospitals, both in government and private sector has been felt. Consequently there has been a proportionate increase in the quantum of waste generated by these health-care centres. Ironically the hospitals hoped to bring relief to the sick are themselves creating health hazards to the community due to improper management of the waste generated in the course of health-care activities. Such waste has been termed as 'Bio-Medical Waste', which according to Bio-Medical Waste (Management & Handling) Rules, 1998 of India means "any waste, which is generated during the diagnosis, treatment or immunization of human beings or animals or in research activities pertaining thereto or in the production or testing of biological, and including categories mentioned in Schedule I"

Though between 75-90 % of the waste produced by the health care institutions is non-risk being generated from administrative and house-keeping/maintenance of health care establishment, the remaining 10-25 % waste is regarded as 'hazardous' and may create a variety of health risks.

Methodology:The study was carried out in Government Medical College Associated SMHS Hospital, Srinagar, J&K.

The data collection was carried out by way of :

a) Observational studies of Bio-Medical Waste in each ward of the hospital, starting from source, handling, collection, transportation, and final disposal.

b) The information / data regarding Bio-Medical Waste Management planning and policies, man-power- their training and safe practices, was collected from the Head of the hospital (Medical Superintendent) of S.M.H.S.Hospital, Srinagar by way of a semi structured interview, proforma being the one used by the WHO Regional Office for South-East Asia, with minor editorial changes.

OBSERVATIONS:

S.M.H.S. Hospital, Srinagar was

Key words: Bio-Medical Waste, segregation

[illegible]

II) The number of persons involved in the collection, handling, and storage of hospital waste, their designation, their training in solid waste handling and management, and the number of years of experience of this type of work.

Number	Designation	Training	Experience
160	Sweepers (Sanitary Attendants)	Nil(non-formal)	Varies, upto 35 years

No instruction / training is given to newly hired waste management staff.

No infection control committee / team exists in S.M.H.S. Hospital, Srinagar

Recommendations for management of Bio-Medical Wastes:

I) Collection:

In plastic bags with rigid ring with the top fold over the rim of dustbin having a lid/ cover. The reusable container should be smooth, well rounded having maximum size of 100 litres for dry waste and 50 litres of wastewater. It should be cleaned and dis-infected regularly should be handled by one person.

Containers/ bags for sharps: Sharps should be collected in separate containers. This special bag should be strong, puncture proof, firmly closed to prevent spillage, falling or leaking out. The container should be provided with a handle.

Garbage collection centre: Covered and protected garbage collection centres should be used for collection of 'general waste'.

II) Storage

i) Central storage area: Prior to incineration on site or prior to transportation for disposal of site, 'clinical waste' is required to be stored, treated separately from 'general waste' storage area and should be clearly identified with clear warning sign. This area should be kept locked with a key available throughout 24 hours for the staff and only authorized persons should be allowed to enter.

ii) Location: It should be constructed away from the hospital building, food preparation & storage area and public places.

iii) Construction: It should be covered, situated on wide drain with impervious hard standing, well lit, well ventilated, and protected from entry by animals and insects.

iv) Capacity: It should contain a minimal capacity of two-day storage.

v) Removal: It should be removed daily for disposal.

III) Handling & Transfer:

The transportation of 'chemical waste off site should be carried out in specially designed vehicles, with a fully enclosed body and a bulk head separating the driver's compartment from the local compartment.

Handler's safety is responsibility of management. Employee should be provided with approved protective clothing and footwear. Training should be imparted to drivers, collectors, and other handlers on risks of the wastes, other instructions, and precautions taken in the event of spillage by accident. These handlers should be protected by vaccinations.

Vehicles / Trolleys for transportation include:

a) Wheel barrow

b) Cycle rickshaw garbage carrier with separate compartments for biodegradable and non-biodegradable wastes

c) Garbage lorry.

COLOUR CODING OF BIO-MEDICAL WASTES:

S. No.	Colour Coding	type of Container	Waste category	Treatment option (as per Schedule I)
1.	Yellow	Plastic bags	Human anatomical wastes Animal wastes Microbiological & bitechnology wastes Solid wastes (items contaminated with blood and body fluids including cotton, dressings, solid plaster, casts, linens beddings, other material contaminated with bolld)	Incineration / Deep burial
2.	Red	Disinfected container plastic bag	Solid waste (waste generated from disposable items other than sharps wastes, such as tubing, catheters, I/V sets, Ryle's tube, urinary catheter, suction catheter, chest drain catheter, blood set , glucose bottles, plastic syringes. (Solid wastes, microbiology and biotechnology wastes)	Autoclaving/Microwaving/ Chemical treatment plus mutilation/shredding
3.	Blue/ (White) translu-cent)	Plastic/puncture-proof containers	Waste sharps (needles, blades, glass etc. that may cause puncture and cuts. This include both used and un-used sharps) Solid wastes (disposable)	Autoclaving/ Microwaving/ Chemical treatment plus mutilation/shredding.
4.	Black	Plastic bags	Discarded medicines and Cytotoxic drugs (waste comprising of out dated, contaminated and discarded medicine) Incineration ash Chemical waste (solid, chemical used in the production of biologicals, chemicals used in disinfection, as insecticides etc. General non-infective wastes Left-over food and peels of fruits.	Chemical treatment and disposal in secured landfills.

IV) Treatment:

Treatment is a process by which waste is modified before it is finally disposed off, so that it can no more act as source pathogens. The main reasons for treatment are to make waste free from micro-organisms, to reduce in volume for better transport and storage, to make part unrecognizable and to convert it more unusable (like syringes and needles)

V) Disinfection:

It is a process of distribution or removal of pathogens that give rise to infection. Hospital waste in category of 'infectious waste' should be disinfected before final disposal as it contains pathological microorganisms responsible for diseases.

The most common disinfectant applicable is 1% sodium hypochlorite.

VI) Disposal:

Final disposal is made by one of the following procedures:

a) Incineration
b) Chemical disinfection
c) Wet (Steam disinfection) and Dry (Screw feed technology) thermal technology
d) Microwave irradiation
e) Land disposal (especially sanitary landfills)
f) Inertization (mixing waste with concrete or other substances before disposal in order to minimize the risk of toxic substance contained in the waste migrating into surface water or ground water.

Formation of Hospital Bio-Medical Waste Management Committee:

The head of the health-care facility should form a Waste Management Committee consisting of following personnel:

1) Head of the hospital / Medical Superintendent (as Chairman)
2) Waste Disposal Officer (as Secretary)
3) Infection Control Officer
4) Head of the Departments
5) Chief Pharmacist
6) Dy. Medical Superintendent
7) Hospital Engineer
8) Radiation Protection Officer
9) Stores Officer
10) Additional members may be appointed whenever the need arises.

The management of bio-medical wastes require diligence & care from a chain of personnel, starting with a nurse or a doctor who use the equipment that become waste, taken by hospital sanitation staff who provide clean bags & containers and carries away the waste, and finishing with the person responsible for ensuring that the bio-medical waste is disposed off in correct way to prevent any damage or adverse effect to the environment and the life sustained in it.

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OBESITY

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Definition: - It is a state of excess adipose tissue mass and an increase in total fat.

Types: - Three types of obesity is known

a) Hypertrophic obesity: - It is due to an enlargement of fat cell size. It is seen in mild obesity.

b) Hyperplastic obesity: - It is due to increase in fat cell number. Commonly seen in morbid obesity.

c) Combination of a and b

WHO CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BMI, WAIST CIRCUMFERENCE AND ASSOCIATED DISEASE RISK

(Disease risk "relative to normal weight and waist circumference.)

	BMI (Kg/ m2)	obesity class	Men =40 in. (102cm) Woman= 35 in. (88cm)	>40 in. (102cm) >35 in. (88cm)
Underweight	<18.5			
Normal	18.5-24.9			
Overweight	25.0-29.9		increased	high
Obesity	30.0-34.9	I	high	very high
	35.0-39.9	II	very high	very high
Extreme obesity	=40	III	extremely high	extremely high

Prevalence:-

Overweight and obesity have reached epidemic proportions in the United States, increasing among all age, race and ethnic groups and in both men and women.

The most recent survey from the National Health And Nutrition Examination Survey (NHANES) for 1999 to 2000 reported the age adjusted prevalence of overweight [defined as BMI =25 Kg/ m^2] as 64.5% and obesity [defined as BMI =30 Kg/ m^2] as 30.5% for U.S adults.

These recent figures represent increases in prevalence of overweight and obesity by 8.6% and 7.6% respectively since NHANES III (1988 to 1994).

In India exact figures regarding prevalence of obesity in not known. However it is estimated that due to unhealthy dietary habits and sedentary behavior during past few decades' prevalence in increasing.

Obesity in the second leading cause of preventable death in U.S. today, accounting for ~ 3 lac deaths/ year. Overweight and obesity pose a major public health challenge. Actuarial tables indicates that life expectancy is decreased when BMI is significantly increased, a BMI of 30 or above is associated with a 50% or higher increase in mortality as compared to a BMI in the normal range (18.5 to 24.9)

ASSESSMENT OF OBESITY

Before we consider assessment of obesity, it will be useful to first look at body composition as under:

a). The active mass (muscle, liver, heart etc.).

b). The fatty mass (fat).

c). The extra cellular fluid (blood, lymph etc.).

d). The connective tissue (skin, bones, tendons and ligaments).

Structurally speaking, the state of obesity is characterized by an increase in the fatty mass at the expense of other parts of the body.

Methods of estimating body fat and its distribution:

Method	Measures Regional fat
1. Height and weight	No
2. Skin folds	Yes
3. Circumferences	Yes
4. Ultra sound	Yes
5. Density	
a) Immersion	No
b) Plethysmography	No
6. Heavy water	No
7. Potassium isotope	No
8. Total water electrical conductivity	No
9. Bio electric impedance	No
10. Fat- soluble gas	No
11. Absorptiometry (DEXA, dual photon absorptiometry)	No
12. Computed tomography	Yes
13. MRI	Yes
14. Neutron activation	No

Best assessment of total body fat
(Dual energy X-ray absorptiometry)

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BI = Height (cm) - 100

BROCA INDEX are widely used. Other methods which were used previously are not used know, they include

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LORENTZ'S FORMULA
CORPULENCE INDEX

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Rapid and Non- invasive test

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d) Physical inactivity: - Physical inactivity may cause obesity which in turn restricts activity. This is a vicious circle.

e) Socio- economic status:- In US obesity is more common in lower Socio- economic strata but in developing countries it is more common in high Socio- economic strata.

f) Eating habits: - Eating habits (e.g. eating in between meals, preference to sweets, taking lot of fats) are established very early in life. The compositions of diet, the periodicity with which it is eaten and the amount of energy derived from it are all relevant to the aetiology of obesity. A diet containing more energy than needed may lead to prolonged post prandial hyperlipidemia and to deposition of triglycerides in adipose tissue resulting in obesity.

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h) Familial tendency: - Obesity frequently runs in families.

i) Endocrine factors: - These may be involved in few cases e.g. Cushing's syndrome, GH def. etc.

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The role of genetics and environment in the etiology of obesity has been evaluated in many studies. Although it varies from study to study ~30% to 40% of the variance in BMI can be attributed to genetics and 60% to 70% to environment. In a given population some people are genetically predisposed to develop obesity, but that genotype may be expressed only under certain adverse environmental conditions, such as high fat diet and sedentary life style.

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Another mouse mutant db/ db which is resistant to leptin, has a mutation in the leptin receptor and develops a similar syndrome.

The recessive obesity (ob) single gene mutation in mouse produces marked obesity and results in a type of diabetes resembling human NIDDM. The mouse ob gene was subsequently isolated by positional cloning. These ob/ ob mice. In addition to being severely hyperphagie, also have a low body temperature. Thus combining increased energy intake due to excess appetite with decrease energy expenditure, leading to explosive weight gain. Furthermore, these animals are infertile suggesting involvement of leptin in hypothalamic pituitary goradal axis. All of these features are reversed by administering mice leptin, the product of ob/ ob gene. Such a treatment also accelerates the outset of reproductive function in normal rodents.

The ob gene is present in humans and expressed in fat. Several families with morbid, early onset obesity due to inactivating mutations in either leptin or the leptin receptor have been described, thus demonstrating the biological relevance of leptin in humans.

The obesity in these individuals begins shortly after birth, is severe and is accompanied by neuroendocrine abnormalities. The most prominent of these is hypogonadotropic hypogonadism, which is reversed by leptin replacement.

To date, there is no evidence to suggest that mutations or polymorphisms in the leptin or leptin receptor genes play prominent role in common forms of obesity.

Anatomical localization of two distinct sets of neurons in the arcuate nucleus of hypothalamus is the key to the understanding of leptin regulated melanocortin pathway. One set of neurons is orexigenic, co- expressing two neuropeptides, agouti related protein (AGRP) and neuropeptide Y (NPY) both of these induce feeding. Leptin action reduces their expression the second set of neurons co- express m-RNA encoding 2 antifeeding (anorexigenic) peptides:-

1)CART & 2)ALPHA-MSH

Laptin induces their expression .Thus Leptin suppresses two orexigenic peptides (NPY & AGRP) & induces two anorexigenic peptides (CART & ALPHA-MSH). It is mainly through these two mechanisms that Leptin affects the melanocortin pathway & inhibits feeding, there by decreasing energy intake.

The receptor mediating the feeding inhibitory action of leptin through these four neuropeptides is the melanocortin receptor (MC4-R) which is primarily expressed in the brain. Activation of MC4-R by a- MSH decreased food intake while suppressions of MC4-R signaling by the endogenous antagonist AgRP decreased the hypophagic response to leptin there by inducing food intake.

Role of PPARγ in obesity

Peroxisome proliferators activated receptor belongs to PPAR subfamily of nuclear hormone receptors. It exits in 2 isoforms, γ1 and γ2 generated from the same gene by alternative promoter usage and m-RNA splicing. High levels of PPARγ2 are almost exclusively expressed in adipose tissue while low levels of PPARγ1 are expressed in many other tissues e.g. liver. Skeletal muscles etc.

Evidence linking PPARγ with obesity:

- PPARγ is rapidly expressed during adipocyte differentiation.
- Forced expression of PPARγ into fibroblast leads to their transformation into adipocytes.
- High levels of PPARγ are maintained in the mature adipocytes.
- PPARγ target genes as lipoprotein lipase and acyl Co A synthetase
- Insulin acutely up regulates PPARγ m-RNA I a dose dependent manner in human adipocytes.
- Thiazolidinedione with bind and activate PPARγ, also induces PPAR? gene expression in rat adipocyte tissue.

Pathogenesis of common obesity

Obesity can result from:-

- Increased energy intake.
- Decreased energy expenditure,
- Or a combination of the two.

4. Increase energy intake:

Energy intake is governed by the appetite of a patient which is itself under control of neural afferents, hormones and metabolites.

Neural Afferents:-

Vagal inputs are particularly important bringing information from viscera, such as gut distension.

Hormones:-

Hormones signals include leptin, insuli, cortisol and gut peptides such as cholecystokinin which signals to the brain through the vagus nerve.

Metabolites:-

Metabolites including glucose can influence appetite, as seen by the effect of hypoglycemia to induce hunger.

These diverse hormonal, metabolic and neural signals act by influencing the expression and release of various hypothalamic peptides that are integrated with serotonergic, catecholaminergic and opioid signaling pathways.

Many abese individuals believe that they eat small quantities of food. However, it is now established that average energy expenditure increases as people get more obese, due primarily to the fact that metabolically active lean tissue mass increases with obesity. Given the laws of thermodynamics, the obese person must therefore eat more than the average lean person to maintain their increased weight. This supports the view that obese person eat more than what they tell on food intake questionnaires.

B. Decreased Energy Expenditure:-

Energy expenditure includes the following components:-

- Resting or Basal metabolic rate.
- The energy cost of metabolizing and storing food.
- The thermic effect of exercise.
- Adaptive thermogenesis (facultative thermogenesis).

Basal metabolic rate accounts for about 70% of daily energy expenditure, whereas active physical activity contributes 5 to 10%.

Adaptive thermogenesis occurs in brown adipose tissue (BAT). BAT expends stored energy as heat. It is defined as heat production in response to environmental temperature or dietary intake. The average total daily energy expenditure is higher in obese than lean individuals when measured at stable weight. However, energy expenditure falls as weight is lost, due in part to loss of lean body mass and to decreased sympathetic nerve activity. When reduced to near normal weight and maintained there for a while, obese individuals have lower energy expenditure than lean individuals.

There is also a tendency for those who develop obesity as infants or children to have lower resting expenditure rates than those who remain lean.

The physiologic basis for variable rates of energy expenditure (at a given body weight and level of energy intake) is essentially unknown. A mutation in the human ß3 adrenergic receptor may be associated with increased risk of obesity and / or insulin resistance in certain (but not all) populations.

One newly described component of thermogenesis, called non exercise activity thermogenesis (NEAT), and has been linked to obesity. It is the thermogenesis that accompanies physical activities other than volitional exercise, such as the activities of daily living, fidgeting, spontaneous muscle contraction and maintaining posture. NEAT accounts for about two thirds of the increased daily energy expenditure induced by overfeeding. The wide variation in fat storage seen in overfed individuals is predicted by the degree to which NEAT is induced. The molecular basis for NEAT and its regulation are unknown.

PATHOLOGIC CONSEQUENCE OF OBESITY

Obesity has major adverse effects on health. Morbid obese individuals (>200% ideal body weight) have as much as twelve fold increase in mortality. People with abdominal or upper body obesity have a greater risk of developing complications of obesity. Men usually have abdominal obesity and women have gluteofemoral obesity but as women gain more weight they also develop abdominal or upper body obesity.

Obesity affects almost all the body systems. Symptoms, diseases and special problems associated with obesity are:-

Cardiovascular System:

- CAD.
- Hypertension.
- Pulmonary embolism.
- Varicose veins.

Gastrointestinal System:-

- Cholelithiasis.
- GERD.
- Colon cancer.
- Hepatic steatosis.
- Hernias.
- Non alcoholic steato hepatits.

Integument System:-

- Cellulites.
- Carbuncles.
- Hygiene problems.
- Intertrigo.
- Venous stasis of legs.

Musculoskeletal System:-

- Immobility.
- Low back pain.
- Osteoarthritis.

Genitourinary System:-

- Hypogonadism.
- Prostate cancer.
- Urinary stress incontinence.

Neurologic System:-

- Idiopathic intracranial hypertension.
- Meralgia paresthetica.
- Stroke.

Psychosocial:-

- Depression.
- Social / Employment discrimination.
- Work disability.

Reproductive / Endocrine Systems:-

- Amenorrhea.
- Breast cancer.
- Cushing syndrome.
- Type- 2 diabetes.
- Dyslipidemia.
- Glucose intolerance.
- Hypothyroidism.
- Infertility.
- Insulin resistance.
- Uterine CA.
- PCOS.

Respiratory System:-

- Dyspnea and fatigue.
- Pick Wickian syndrome.
- Obstructive sleep apneas.

Proportion of disease prevalence attributable to obesity:-

Disease	Prevalence (%)
Type- 2 diabetes	61
Uterine cancer	34
Gall bladder disease	30
Osteoarthritis	24
Hypertension	17
CAD	17
Breast cancer	11
Colon cancer	11

DISORDERS ASSOCIATED WITH OBESITY

1. Insulin Resistance and Type-2 Diabetes:-

Hyper insulinemia and insulin rest. Are common features of obesity, increasing with weight gain and diminishing with weight loss. Insulin resistance is more strongly linked to intra abdominal fat than to fat with other deposits. Factors responsible for insulin resistance are:-

a) Insulin: - Insulin itself induces down regulations of its receptors.

b) FFA: - FFA is increased in obesity and impairs insulin action.

c) TNF-α: - It is produced by adipocytes. It is overexpressed in obese adipocytes and capable of inhibiting insulin action.

Obesity is a major risk factor for diabetes and as many as 80% of type-2 diabetics are obese weight loss even of modest degree, is associated with increased insulin sensitivity and often improves glucose control in diabetes.

[illegible] phospholipids [illegible]

[illegible]

morbidly obese group.

[illegible] peripheral [illegible] women with [illegible]

[illegible] drugs [illegible]

restore normal menses.

[illegible] androgen [illegible]

[illegible] incidence [illegible] associated [illegible]

Gall bladder.

CARDIOVASCULAR DISEASE

FRAMINGHAM STUDY [illegible]

[illegible] 26 year [illegible] independent [illegible] cardiovascular [illegible]

[illegible] men and women.

[illegible] Ovarian [illegible]

[illegible] women [illegible]

[illegible] VHDL and HDL [illegible] cholesterol.

[illegible] insulin resistance [illegible] peripheral [illegible]

[illegible] output; increased [illegible]

[illegible] sensitivity [illegible]

[illegible] Assessment of the weight [illegible]

The most important goal in the assessment [illegible]

PULMONARY DISEASE [illegible] decide whether [illegible]

[illegible]

[illegible] is indicated. Whether treatment is indicated [illegible]

[illegible] Whether treatment [illegible]

[illegible] is ready and Whether the patient [illegible]

[illegible] ventilation [illegible] due to [illegible]

[illegible] BMI of 30kg/ m2 [illegible]

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

rarely succeed in a weight - loss program. Patients at low moderate risk who are not ready to lose weight should be urged to maintain their current weight. A healthy life style should be encouraged and any complications of obesity should manage appropriately. Patients at high risk should educate about the benefits of weight loss, with the goal of motivating them while maintaining a therapeutic alliance.

MANAGEMENT OF OBESITY AS A CHRONIC DISEASE

The successful management of obesity requires a long term approach that is tailored to an individual's life style and needs. According to evidence based guide lines from a National Institute of Health (NIH) expert panel, treatment is indicated for obese patients with a body mass index of 30kg/ m2 or higher as well as for overweight patients with BMI of 25- 29.9 kg/ m2 (or a high waist circumference) plus two or more risk factors. The initial goal is to lose ~ 10% of body weight and once this is achieved, further weight loss can be considered if indicated.

To maintain weight loss the individualized program should be continued indefinitely. Management program is discussed under three broad headings:

1. NON PHARMACOLOGIC TREATMENT OPTIONS.
2. PHARMACOLOGIC TREATMENT.
3. SURGICAL OPTIONS.

NON PHARMACOLOGIC TREATMENT OPTIONS

The initial treatment of obesity should focus on a diet and exercise program that has been individualized to the patient's life style and physical needs. Behavioral therapy should be implemented as an adjunct to this program.

A. Nutrition and Diet

Reduced caloric intake is the corner stone of obesity treatment. The fundamental goal is the sustained reduction of energy intake below that of energy expenditure. Many different types of diets have been recommended for promoting weight loss, but regardless of which diet is selected, the total energy intake must be reduced in order to weight loss to occur. More over once weight loss has occurred, the lower energy intake must be sustained to prevent weight regain.

Caloric restrictions of 500 to 600k cal/ day generally lead to weight loss of 0.5kg per week and a 10% decrease in weight by 6 months.

a)Very low energy diet

During 1970's liquid protein were popular, but they proved to be unsafe causing >60 deaths. Life threatening arrhythmias were documented in the clinical research setting, a consequence of both low quality protein and deficiency of vitamins, minerals and trace elements. These types of diets have now been modified.

A very low energy diet (e.g. 400 to 600k cal/ day) consisting of 45 to 70g high quality protein, 30 to 50g. Carbohydrate and approximately 2g fat per day as well as supplements of vitamins, minerals and trace elements appears to be safe in selected patients under medical supervision.

Contra indications to this diet include

- Pregnancy.
- P.
- Cancer.
- Recent MI.
- Hepatic disease.
- Untreated psychiatric disease.
- Renal disease.

Advantages of very low energy diets

- Greater rate of weight loss.
- Beneficial effect of hunger suppression brought about by ketone production.
- Good control of BP, blood glucose, cholesterol and TG's.
- Pulmonary function and exercise tolerance improve with in a few weeks.
- Sleep apnea also improves with in a few weeks.

Complications of these very low energy diets

There are minor and include:-

I. Fatigue.
II. Consumption or diarrhea.
III. Dry skin.
IV. Hair loss.
V. Menstrual irregularities.
VI. Orthostatic dizziness.
VII. Difficult concentrating.

Cholelithiasis and pancreatitis may occur when such diets are interrupted by binge eating; gall stones have been shown to develop in as many as 25% of patients while on diet.

Very low energy diets have been used successfully in patients with morbid obesity that was unable to undergo elective surgery because of their weight.

b) Low energy diets, >800k cal/ d to 1200 k cal/ d

This diet is applicable to most patients and has fewer restrictions than the very low calorie diets. Considerable controversy has attended the question of which diet composition is most appropriate for promoting weight loss. A diet rich in fruits, vegetables and whole grains may promote weight loss and is preferable to low- fat diets in which large amounts of simple carbohydrates are substituted for fats.

B. Physical Activity

Since obesity is associated closely with a sedentary life style, exercise is a potent physiological stimulus for lipolysis, which results in the release of free fatty acids from triglycerides stored in fat for use as an energy source by muscles.

Although exercise alone may produce a 2% to 3% reduction in BMI, it is most effective when used as an adjunct to dietary therapy.

A starting programs for obese patients of 30 to 45 minutes of moderate physical activity should be encourage at least 3 days per week, and if possible, it should be performed on most days. Exercise is also valuable in obese patients for its effects on cardiovascular tone and blood pressure.

C. Behavioral Modification

Behavioral strategies are designed to change the patient's eating and activity habits. These strategies are an important component of a weight loss program because they target the barriers that often limit patient adherence.

Behavioral modifications therapy is usually conducted in a

[illegible]

cholesterol loss.

ORLISTAT PHARMACOTHERAPY

[illegible]

Recombinant human leptin [illegible] in the rare cases of [illegible] leptin gene [illegible]

[illegible] limited or absent in [illegible] disease.3.

SURGERY

[illegible] patients with BMI >40 kg/m2 [illegible]

[illegible]

Vertical Banded Gastroplasty [illegible] a restrictive pouch with a [illegible] lesser curvature of stomach [illegible]

Roux-en-Y Gastric Bypass

[illegible] pouch is constructed [illegible] shaped limb of the small intestine [illegible] following gastric bypass [illegible] (100lb) or 100% [illegible]

weight. Mazindol

[illegible] of other therapeutic approaches [illegible] capability of [illegible] alcoholism and other addictions [illegible] psychiatrist. Prior clearance by [illegible]

POST EXPOSURE PROPHYLAXIS FOR HEALTH CARE WORKERS

Sameena Farhat MD; Zaffar Abbas MD.

COMMENT

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JK-Practitioner2004;11(3):217-218

Continuing training of physician devoted to HIV care is crucial to their optimal management of patients, Recent congressional threats to the funding of the education and training centers, federal program to train medical professional in HIV care may effect the ability of many providers to receive state of the art medical information. AIDS training programmers can improve practice patterns and result in better health care outcomes for AIDS patients.

Relevant to subject is post-exposure-prophylaxis for health care workers. The network starts from out patient care hospitalization-substance abuse treatment-home care-emergency care-hospital care-case management-clinical trials-nutrition services and finally seeps to "PEP" (Post Exposure Prophylaxis).

The US based health services (CDC) after spending long time over the subject have come up with certain recommendations on using antiviral agent as "Post exposure prophylaxis" to prevent HIV infection in health care workers exposed to virus on the job. The detailed report related stands issued[1] and updated[2].

The agency first classified HIV exposures by levels of risk and then examined the value of using the various available medication at the different risk levels, while deciding the drug efficiency compatible to risks/ exposures.

The levels of risks are proposed to be based on two factors:

- Type of exposure
- Type of HIV infected source material.

Obviously the highest risk exposure subjection is directly related to "Percutaneous" which in the plain term tantamount to exposure to a contaminated needle.

The second risk from mucous membrane exposure and source related to such type of risk is mouth or eyes.

Besides above, lowest risk cannot be isolated without definition, when it is clear and proves lethal to humans in terms of splashing of HIV contained material on skin.

The most risky source material was blood from an HIV-positive person particularly if large volumes of blood were involved, or if the source person was experiencing either late stage AIDS or initial HIV infections.

Lower risk source include other potentially infections body fluids (such as semen, vaginal secretion and internal fluids including amniotic fluids). while the source least likely to spread HIV was such fluid as urine and saliva.

The highest risk scenario-Percutaneious exposure to HIV-Tainted blood-has an average 0.3% risk of HIV transmission.

Initially the choice offered was ATZ, (Zidovudine) because this is the only drug for which substantial data exist for recommending its use. Retrospective introspection over the vital issue indicate that it reduced the risk of occupational HIV transmission by 97%. Then (Lamivudine) 3TC [illegible] because a [illegible] kind of people with [illegible]

[illegible] transmission if [illegible] inhibited more [illegible]

[illegible]

[illegible] PEP's [illegible] started late the PEP's [illegible]

[illegible] than AZT alone [illegible]

[illegible] infection during primary HIV infection [illegible]

[illegible]

[illegible] individual long-term prognosis [illegible]

[illegible]

[illegible] are recommended are [illegible]

[illegible] HIV [illegible]

established HIV

[illegible] interaction [illegible] drug [illegible]

[illegible] for which [illegible] The length of time for which [illegible]

[illegible] thought to have [illegible]

[illegible] is unknown. [illegible]

[illegible]

[illegible] a safe bet for prevent [illegible]

[illegible] ZT-resistant strains [illegible]

[illegible] States recommendations [illegible] Vol [illegible]

[illegible] Health Service [illegible]

[illegible] of

[illegible] worker exposure to HIV [illegible]

[illegible] exposure prophylaxis [illegible]

[illegible] after [illegible] exposure. [illegible]

(RR-7): 1-28.

[illegible] March 2003 [illegible] guidelines [illegible]

[illegible] Public Health [illegible]

[illegible] HIV and [illegible]

[illegible] prophylaxis [illegible]

1-42. [illegible] 2001 (June): 50(RR-11): 1-42.

[illegible] HIV prophylaxis following [illegible]

[illegible] reduce [illegible] prevalence of HIV [illegible]

PROGRAMMED CELL DEATH (APOPTOSIS) PHYSIOLOGICAL & PATHOLOGICAL SIGNIFICANCE

Ashfaq-ul-Hassan MBBS, Mohd. Shafi MS, Ghulam Hassan MS

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Derived from a greek word meaning falling off. Also called cell suicide, Apoptosis or the programmed cell death is one of the most challenging and widely studied topics currently. The phenomenon is of prime importance right from embryological fusion of two cells till the death of an individual. In the continuous process of life this process is seen to have a fundamental role. The homoestasis of an organism requires a perfect equilibrium between the generation of new cells and death of older ones. The death of cells occurs as a result of trauma, hypoxia, heat, ultravoilet irradiation, viral infection, other intracellular pathogens etc. In the process of apoptosis cell death is genetically programmed. The cells own genes play a role in cell demise. For some cells to live and sustain others have to die. This is the best possible example of cellular cooperation. In other organisms cells are shed as they come to the end of their life span. Apoptosis tends to effect specific cells. It is an energy dependent process. The cell chromatin is broken down by are activated which ultimately lead to cell disruption and cell death. These dead cells may be shed from free surfaces, others phagocytosed by macrophages etc to form apoptotic bodies. New surface molecules appear on apoptotic cells which help in their recognition and subsequent phagocytosis. Unlike necrosis there is no inflammatory response and this under lines the physiological nature of the process. Apoptosis is prominent during Emroygenesis. Initiation of Apoptosis is regulated by growth factors some turning it on while others delaying or preventing it.

Apoptosis can also be a pathological process found in tissues undergoing atrophy or tissues irradiated. It is an important factor in controlling rate of growth in tumors.

Apoptosis can be mediated by both intracellular or extracellular signals. Intracellular mechanisms activate enzymes causing disruption of cellular architecture, cell shrinkage and finally cell death. Extra cellular mechanisms act through TNF receptors or indirect activation of intracellular mechanisms leading to cell death.

Abnormal apoptosis leads to auto immune diseases, neurodegenerative diseases and cancers.

Text:

In the normal development of an individual it is essential that there is a proper balance between regulation of normal cell growth and cell death. Excessive supression of cell death by apoptosis can otherwise be an important determinant of growth of cancers. In addition apoptosis serves in deleting abnormal cells damaged by toxins, radiations or other mechanisms. The apoptotic cells undergo through a highly sophisticated and monitored pathological sequence of events. The main steps involved are:

Cell Shrinkage
Chromatin condensation
Formation of cytoplasmic blebs and and apoptotic bodies
Phagocytosis

Histologically in tissues stained with hemotoxylin and eosin, apoptosis involves single cells or small cluster of cells. The apoptotic cell appears as round or oval mass of intensly eosinophilic cytoplasm with dense nuclear chromatin fragments. Apoptosis is unique in the fact that it doesn't set an inflammotory reaction and hence making it more difficult to detect it histologically.

Apoptosis is a common process seen during embryogenesis in all steps such as implantation, organogenesis, development involution and metamorphosis. The separation of digits during the limb development is a classic example of effect of Apoptosis in

Key words: Fracture, First Rib, Congenital fusion

Embryology. The regression of the duct systems in the course of sexual development of fetus is attributed to this mechanism only. The Mullerian inhibiting substance (MIS), a member of TGF beta super family of growth factors causes regression of mullerian ducts, hence promoting sexual development in humans. During the development of Central Nervous System active remodelling occurs during synapse formation, large number of neurons are produced and some die. Apoptosis plays a role in preserving most effective neurons. In early life the same mechanism helps to get rid of inappropriate clones of lymphocytes. Even death of B&T lymphocytes and deletion of auto reactive T cells in thymus is a result of apoptotic mediation.

The role of Apoptosis in the adult is recognized by the fact menstrual initiation genetically predetermined programming in females occurs at menarche leading to a periodically alteration in the levels of estrogen and progesterone triggering synhronous Apoptosis. This causes endometrial cell breakdown and onset of menstruation. The breast is seen to undergo proliferative changes during pregnancy. But once the pregnancy is over and a new born starts weaning and the use of breast as a nutritional source seems to diminish, a gradual regression of changes sets in the breast tissue. All these changes are automatically coordinated by a complex cascade of events, hormonal changes etc. but meiated by apoptosis.

The mucosae of the intestine is a highly active independent system undergoing high activity. The mucosal cells undergo a hectic wear and tear mechanism and like other tissue such as bone marrow these cells are known for their rapid turn over rates. The worn out cells are shed and death of these enterocytes occurs. This mechanism is especially seen in autoregulatory mechanism such as maintenance of iron absorption. In iron overload the intestinal mucosal cells containing iron are shed by mechanisms similar to apoptosis where it is not necessarily genetically predetermined.

In the erythrocytes, Erythropoetin is responsible for increasing the number of committed stem cells which form the R.B.C.s when erythropoetin levels are low, Erythroid stem cells show DNA clevage followed by apoptosis. Normally this reduces DNA clevage and causes cells to survive. Loss of this erythropoetin regulation over apoptosis leads to shortening of R.B.C life span considerably.

In various infections such as certain types of viral hepatitis it is seen that single scattered liver cells die one by one. These cells become eosinophilic with a pyknotic nuclueus which is eventually extruded out leaving besides a acidophilic or councilman body.

The main mediators of apoptosis are:
Endonucleases
Proteases
Trans glutaminases
Vitronectin receptors
Bcl-2 oncogene
c-myc oncogene
p-53
Ced-9 gene
Ced-3,4 gene

Cancers are more common in tissues with rapid cell turn over & those tissues whose proliferation is regulated by hormones and those exposed to environmental carcinogens. Most common genetic changes involve activation of proto oncogenes and inactivation of Tumor suppressor genes. Apoptosis has an effect on expression of these genes also. Hence on cancer development as well. The expression of carcinogenesis as a multiple step process is well established. Capacity to metastatize, due to proteases, neovascular proliferation, bypass immune survellance mechanisms, down regulate Major histocompatibility Complex Antigens etc are all mediated by apoptosis e.g., simple alterations in p-53 gene can lead to a variety of human cancers which may be genetically predetermined such as Li-Fraumeni syndrome, sarcomas, Lymphomas, Leukemias, Breast tumors, adrenal tumors, etc.

The neuro degenerative diseases such as Parkinson's Disease, Alzhiemers Disease, Huntigtons Disease, Amyotrophic Lateral sclerosis etc. follow a characteristic pattern of neuronal degeneration which is progressive and irreversible.

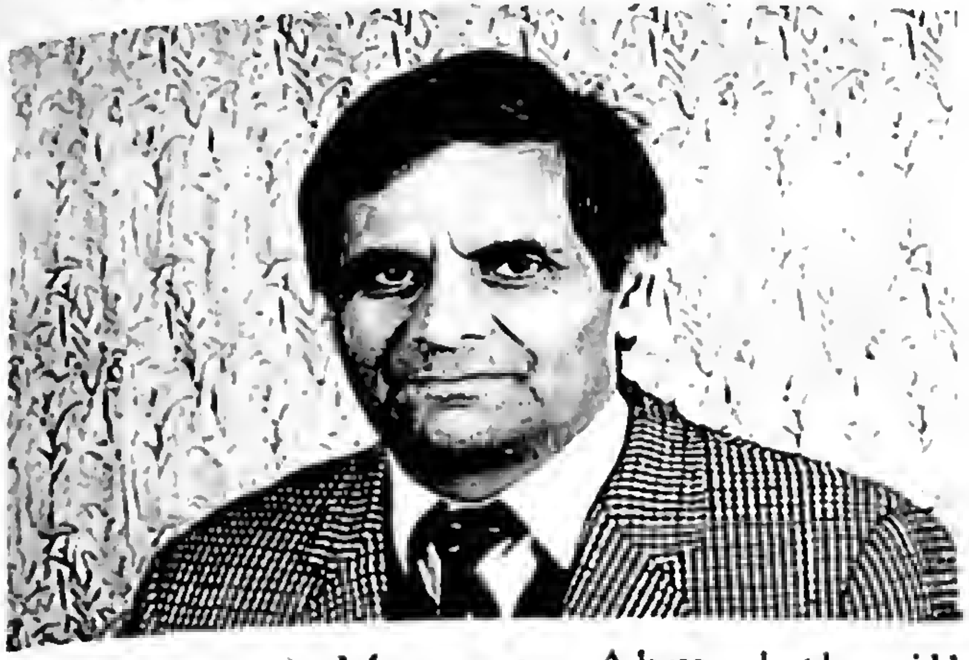
Apoptosis is a genetically encoded programme and apoptosis may occur after irradiation induced cellular damage in normal or tumor cells by activation of endogenous nucleases Fragmentation of DNA, loss-of cell integrity. Mutations of p-5-3 may cause the tumor cells to undergo programmed cell death.

In septic shock the heat shock proteins are involved in apoptosis. Normally these make cells more resistant to stress but their over expression may be deleterious. Here these proteins may adversely effect mechanisms like folding, stabilizing and translocation proteins and eventually causing cell death.

In cerebal ishaemia, due to atherosclerosis, vasculitis, embolic phenomenon, Vasoconstriction etc. damage to DNA portions, fatty acids as a result of free radicals, acidosis etc. is induced by programmed cell death and neuro protective drugs aimed at halting those mechanisms are being developed.

MANZOOR AHMAD

(11 March 1940 – 3 March 2004)



Prof. (Dr.) Manzoor Ahmad the illustrious ophthalmologist of Kashmir died suddenly of a cardiac ailment at SKIMS in Srinagar. He was 64 years of age. At the time of his death he was successfully running a private Eye Hospital at Wazir Bagh, Srinagar. In a career of 40 years as an ophthalmologist Dr. Manzoor made significant contributions to the development of ophthalmology at GMC, Srinagar. For J&K he has many firsts to his credit-was the first to perform retinal surgery in 1973, first to perform Fluorescein Angiograpy & Retinal photocaogulation in 1978 and first to perform Laser Traberculoplasty in 1993. He is also credited with starting the post-graduate course (MS) Ophthalmology in Govt. Medical College Srinagar in 1989.

He performed the first Trabeculectomy in North India in 1974. He was also the first to implant Intra ocular lens for cataract in India in 1979.

After completing his MBBS from MGM Medical College, Indore in 1962 he pursued his specialist training in Ophthalmology from the same College. A keen sportsman he would often start his day from the golf course. His love for cricket and regular presence on the Lawn Tennis Court of Amar Singh Club in his earlier days is known to all.

His pursuit for learning and attaining excellence in his skills made him to seek knowledge in places like Germany, London and the USA. Fellowships in Retinal Surgery (Germany 1972), Cataract (London 1973), Glucoma (Germany 1975) and cataract Surgery (Florida USA) honed his skills to perfection. Scores of publications in reputed journals and presentation of papers in national and international forums made him a well known academician. He has done pioneering work in the field of Exfoliative Glaucoma and intra ocular Lens in Fuchs Cyclitis.

Dr. Manzoor joined the faculty at Govt. Medical College as Assistant Professor in 1965 and became the youngest Professor ever at GMC, Srinagar, in 1974 contuining on this position till 1989. He took voluntary retirement thereafter to establish his own Valley Eye Hospital.

My first interaction with him was when I appeared for the registrar interview. I did well He was impressed and there was no looking back for me. If I have imbibed half of his sense of discipline, his dedication towards the job at hand and his pursuit for perfection. I will consider myself an asset to the society.

He was gentle but firm with collegues, open to ideas but made his own decisions, respected the authority but did not prostrate before it. When I ventured to ask him about the reason for early voluntary retirement from Govt. Service, fearing that a brush with authorities may have promoted the decision the answer was a categoric No." I want to establish a EYE HOSPITAL in the Valley. I may not be able to do it after 10 years" That was Dr. Manzoor who always made his decisions and then made sure to give his best to bring them to conclusion. Perhaps the decision to donate his eyes carried faithfully after his death was an outcome of his firm conviction.

He made it a point to attend the "Annual Dinner" of the Medical Faculty Association where the ex-faculty are invited. His characteristic walk, polished manners, perfect dress sense were always an inspiration for the new and the old assembled there.

Dr. Manzoor is survived by his wife, two sons and a daughter. His eldest son Dr. Khurshid is an ophthalmologist.

I will always pray for him.

Prof. A.R. Nasti
Head, Deptt. of Ophthalmology,
Govt. Medical College, Srinagar.

M L KOUL

(1928 – 2004)

In turned out to be a sad April day when the news of passing away of Prof. ML Koul reached me. The very room where he carried the affairs of the department with authority for 14 long years was a place for me and my collegues to mourn his death.

Dr. Koul did his MBBS in 1960 from Bombay University and also completed M.Sc (Anatomy) from the same institution in 1963. He headed the department of Anatomy at GMC, Srinagar from 1965 to 1976 and then again from 1980 to 1983. During these years he established the department of Anatomy and transformed it into one of the well knit unit of the institution. He did similar work in Jammu from 1977-1980 where he was transferred on establishment of a new medical college there. He retired from government service in 1983. After serving in Libya for six years (1984-1990) Dr. Koul returned to the valley in 1990 to take up the responsibility of setting up the department of Anatomy at JVMC in Srinagar. He has authored "Compendium of Anatomy"- still a must in the bookshelves of the students of Anatomy.

He was an excellent and impressive teacher and a very able administer and played positive part in establishing the department of Anatomy in GMC Srinagar, GMC, Jammu and at the JVMC Srinagar. A towering personality he stood out in the corwd-be it the Anatomy dissection hall or the sports field.

Prof. Kulbir Kour
Head, Deptt. of Anatomy
Govt. Medical College, Srinagar.

CORRECTIONS TO THE ARTICLE JK-PRACTITIONER 2004 VOL. 11 (2): 144-148.

Page No.	*Subject*	*Word Shown*	*To be Read As*
145	Methods and results(e)	1800 00	180° 0°
145	Methods and results(f)	00 1800 00-3600	0° 180° 00-36°
147	Tissue air ratio (TAR)	Abs. dose in a phantom with d cm. of over lying tissue. Abs. dose at the same point with just enough phantom build up material	$\dfrac{\text{Abs. dose in a phantom with d cm. of over lying tissue.}}{\text{Abs. dose at the same point with just enough phantom build up material}}$

The following figures were missed (refer page 146 of the article)

Fig.1a

Radiation Device: Theratron-780E Energy: 1.25MeV Field Size at SAD: 100x100 mm SSD: 800 mm
Wedge: 0Degr. Gantry Angle: 0 Degr. Coll. Angle: 0 Degr.

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Level 20 %

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Level 80%

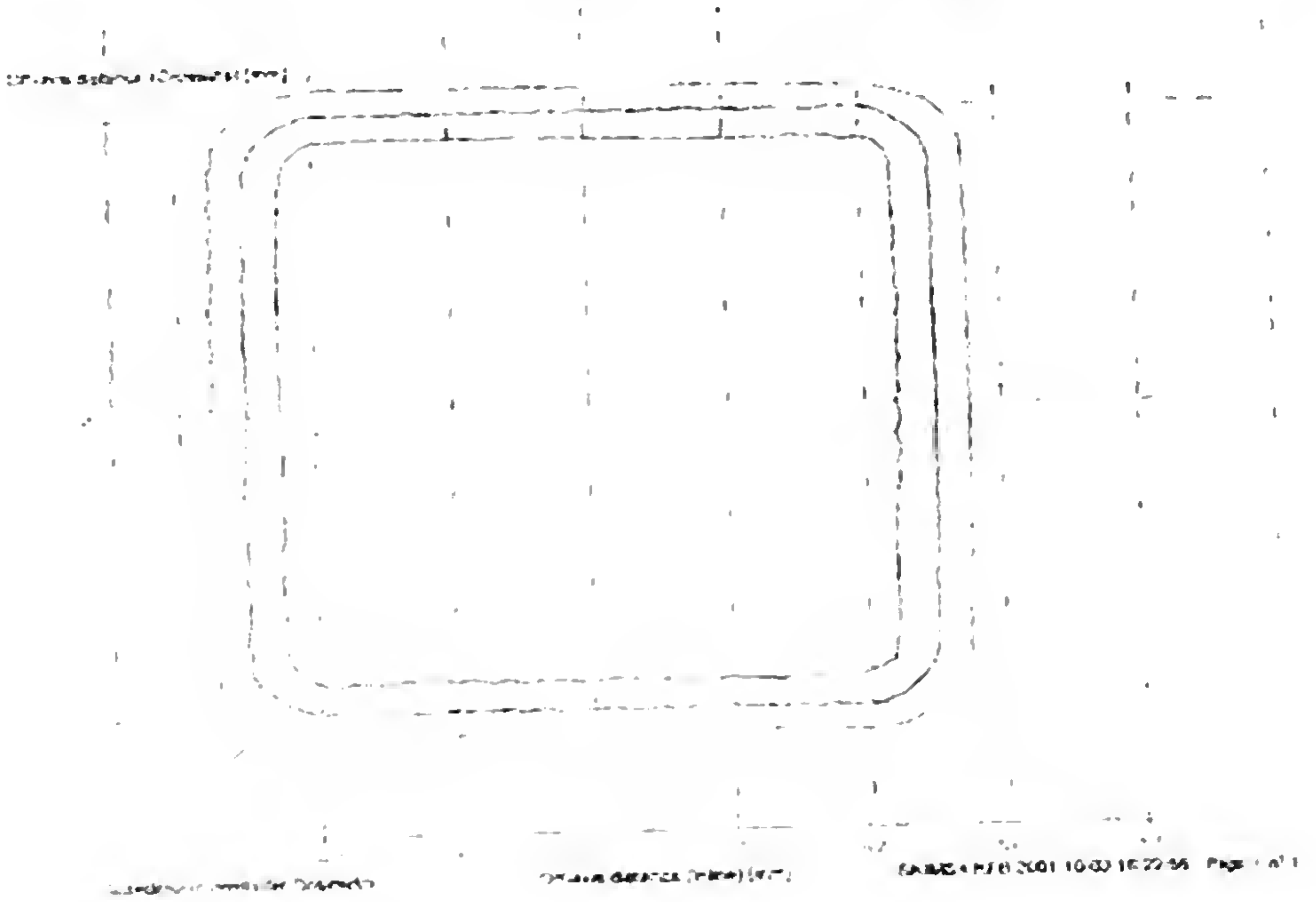
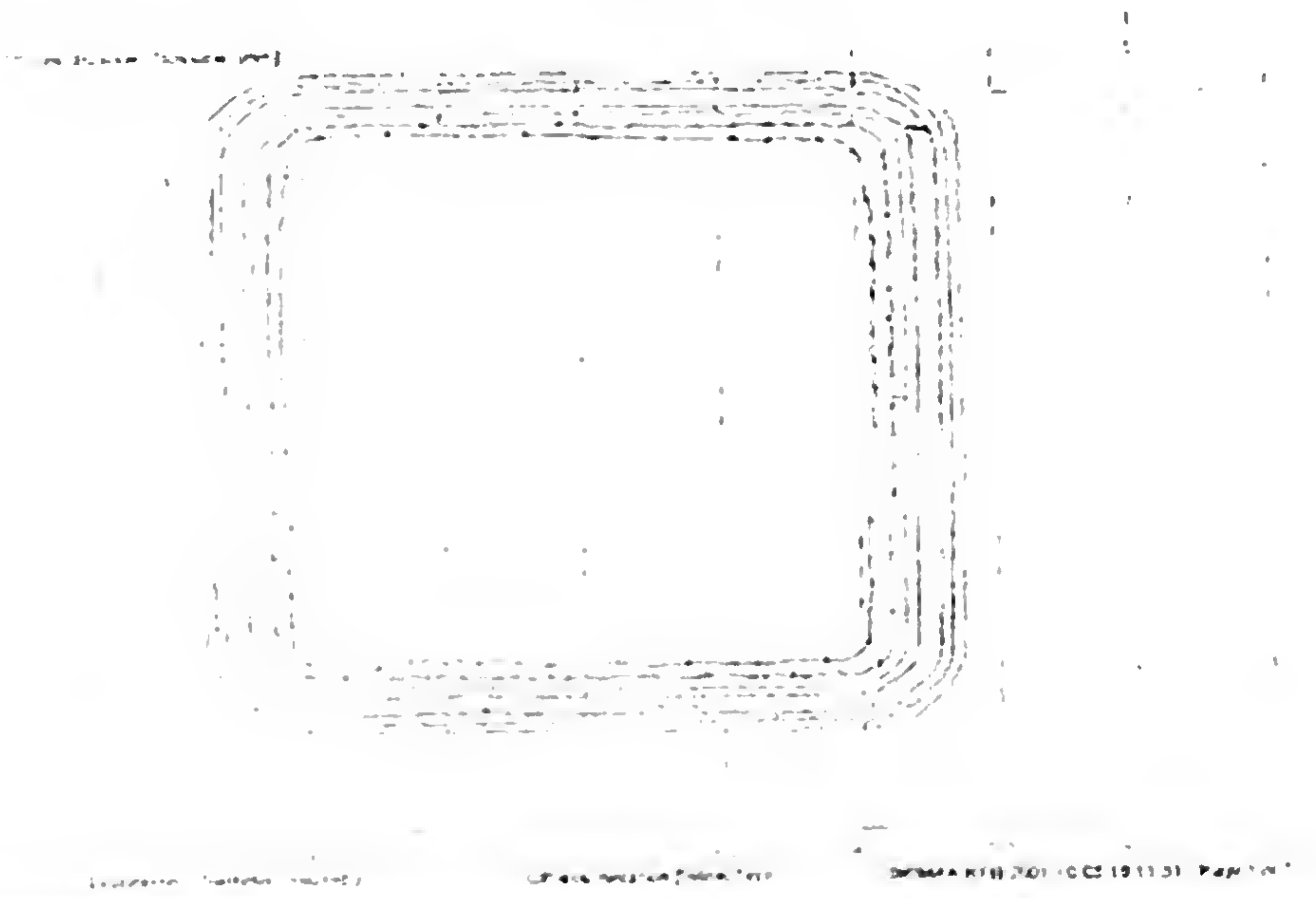


Fig.1b

Radiation Device: Theratron-780E Energy: 1.25 MeV Field Size at SAD: 100x100mm SSD: 800mm
Wedge: 0 Degr. Gantry Angle: 0 Degr. Coll. Angle: 0 Degr.



TOWARDS GREATER INTEGRATION: MARKING MENTAL HEALTH WEEK

There is a call to revolution this week, not only must we change the way mental illness is treated, we must change the very understanding of it. The astronomical monetary costs, let alone tragic human costs, associated with it demand nothing less.

Mental Health week is an event held annually to promote tolerance and understanding of mental health issues. Mental Health week is being celebrated from Sunday the 4th of October to Sunday the 10th of October 2004 and also incorporates World Mental Health day, which falls on 10th of October. This year the theme for Mental Health week is "resilience". This theme was chosen as it depicts the strength and spirit of those affected by mental illness. The stress is on promoting community awareness by providing education of the issues towards greater understanding and empathy for those affected by mental illness. During the Mental Health week we must as a community focus our energies on improving the quality of life and opportunities of all individuals with mental illness and send a message of hope and inclusion to the community at large. Psychiatric disorders are shockingly common, they affect almost every family and are truly non discriminating in their presence in rich and poor, male and female, children and adult, Christians and Hindus or Muslims. Yet the stigma associated with mental illness keeps it largely hidden.

Initial estimates suggest that 450 million people alive today suffer from psychiatric disorders. Major Depressive Disorder is now a leading cause of disability globally and ranks fourth in the leading causes of global burden of disease. 140 million people suffer from substance use disorders, 50 million have epilepsy, another 24 million have schizophrenia, a million people commit suicide every year, between 10 - 20 million attempt. Among the first ten leading causes of disability due to disease world wide six are purely psychiatric disorders. Besides we are living in a conflict zone were loss of life and property, social disorganization and psychological trauma has been enormous[1]. The potential for psychological sequel is considerable. Minimizing the impact and managing the psychological aftermath of repeated severe traumatic stresses is matter of alarm for all the concerned particularly mental health care professionals. Several strategies need to be employed if the goal of acceptance and inclusion is to be realized.

The integration of Mental Health with General Health Care is the first logical step for the accomplishment of goal and will not only end vows of thousands of mentally ill but will also avoid shame, stigma and exclusion associated with mental illnesses. The scope for making mental health care an essential component of primary health care is a universal need .The real beginning for providing services out side mental hospitals in India can be traced to the setting up of General Hospital Psychiatric Units (GHPU) in the 1960's. The emergence of these units in general hospitals led to a complete change in the whole approach to psychiatric treatment. It also contributed significantly to the increased awareness' among mental health professionals and non-psychiatrist physicians regarding the importance of detecting and treating psychiatric disorders in the physically ill. GHPU has also provided an opportunity to remedy the unfortunate situation of imparting exclusive mental hospital centered training in place of a well structured integrative postgraduate program which can enable students spend at least half of their training period in general hospitals to get fully prepared to meet the problems in the world outside.

Second the process of shifting care from the confines of mental hospital to the community needs to be taken up as one of the topmost priorities by all the healthcare planers and other concerned agencies. The community will need to confront the stigma and lack of awareness that exists around mental illnesses, to challenge the discrimination that individuals with mental illness often encounter and to ensure that support services and treatment are available and accessible in every community[2]. District Mental Health Program (DMHP) launched at national level during the last decade (1990-2000) if implemented as it should be, can go a long way in making these goals achievable, as it envisages:

"a community based approach to the problem ,which includes (i)training of the mental health team at the identified nodal institutes within the states;(ii)increase awareness in the care necessity about mental health problems;(iii)provide services for the early detection and treatment of mental illness in the community itself with both OPD and indoor treatment and follow-up of discharged cases and(iv)provide valuable data and experience at the level of community in the state and centre for future planning ,improvement in services and research. NMHP (GOI,2000).

Public mental health education through media, especially news papers and magazines, radio, television can also facilitate community mental health activities.

Last of all, mental health reform must transform an overly protective, over burdened and paternalistic service delivery system into one that is client centered. A reformed system **"client fist perspective"** that recognizes the individuals as an equal partner in the health care system and that involves the individuals in all decisions that affect their care, life and treatment. The individual must be able to retain responsibility for his own wellness and recovery and to have his decision and choice respected. Anything less will mean that mental health reform has been a failure. Since every society to which an individual belongs has its indigenous harmonizing and coping mechanisms which need to be reinforced and developed into innovative scientific modules appropriate to the specific sociocultural perceptions and processes of the masses .In this context, the editorial remarks of Prof. N N Wig- one of the pioneers of mental health movement in developing countries in general and India in particular, published by Indian journal of psychiatry in 1978 "as is not uncommon in our country, minor scientific innovations in Europe or America becomes a major preoccupation of academic circles while major indigenous development (like involvement of families in treatment of psychiatric patients by Vidya Sagar in Amritsar and others in Vellore and Banglore) for more than two decades, often go unnoticed. We seem to stand and wait till a foreign expert comes and tell us which development is good for us, before we dare to recognize it"[3] even after twenty six years are equally enlightening and thought provoking today.

During Mental Health week lets begin implementing the dream restoring hope and demanding a reformed mental health system that is need based, accountable and available to the people it is intended to serve. Together we can accomplish great things with and for all individuals with a mental illness.

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JK - Practitioner 2004; 11(4):223-224

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JK-PRACTITIONER

PERIPHERAL ARTERIAL DISEASE - THE SILENT KILLER.

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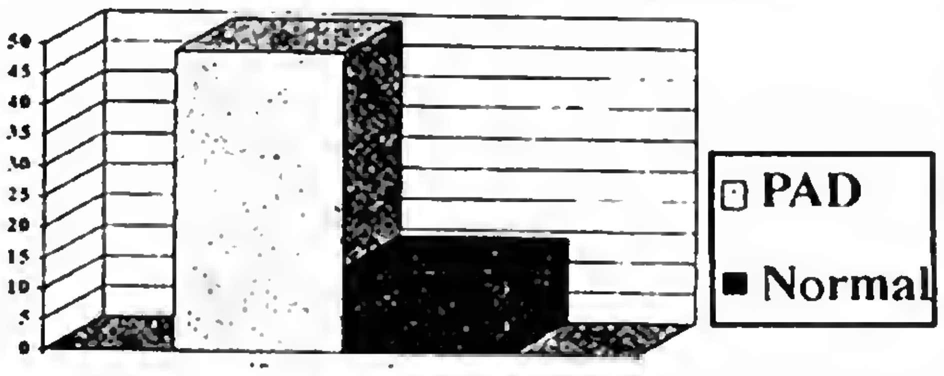
JK-Practitioner 2004; 11(4):225-232

Peripheral arterial disease is an atherothrombotic syndrome associated with high mortality secondary to cardiovascular and cerebrovascular ischemic events[1].(Figure 1) Although the definition of PAD includes diseases within the extracranial carotid arteries, the upper extremity arteries, and the renal and mesenteric circulation, in this review we will focus on the chronic occlusive arterial disease of the lower extremities. Most of the patients with peripheral arterial disease of the lower extremities are asymptomatic. Those with symptoms can present with intermittent claudication or rest pain with or without tissue loss, so called "critical limb ischemia (CLI)". Several community surveys have clearly highlighted the fact that despite being a very highly prevalent disease, physicians under-diagnose and under-treat PAD[2]. This led to the Executive committee of the Prevention of Atherothrombotic Disease Network to issue a "call to action" citing critical issues in peripheral arterial disease detection and management[3]. This group has recommended five measures to address PAD as a significant global public health concern, which are summarized in Table 1.

10 year mortality in PAD partients as compared with normal



10 year mortality
Criqui MH[1]

Figure 1
10 year mortality in PAD partients as compared with normal
Source of data :
Criqui MH et al.[1]

Table 1. Call to Action:

1. Increase awareness of PAD and its consequences
2. Improve the identification of patients with symptomatic PAD
3. Initiate a screening protocol for patients with high risk for PAD.
4. Improve treatment rates for patients diagnosed with symptomatic PAD.
5. Increase the rates of early detection among the asymptomatic population.

The current article is based on the reviews and articles on the epidemiology, assessment, and medical treatment of peripheral arterial disease, which were published in the last year.

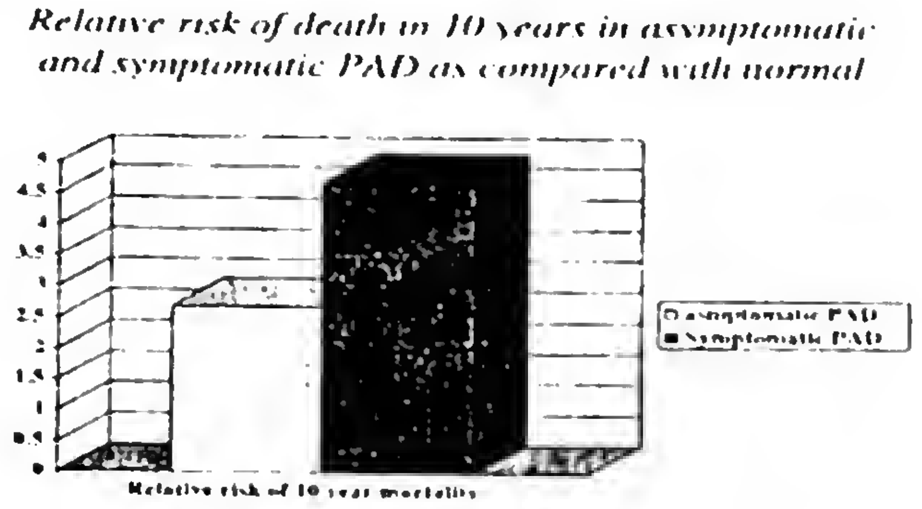
EPIDEMIOLOGY

Peripheral arterial disease is a progressive disease, which has a variable prevalence depending on the method of diagnosis, age, sex, race and the geographic area. Studies using intermittent claudication as a marker of PAD highly underestimate the prevalence, as more than 70% of the patients with PAD are asymptomatic[4]. Although the risk of limb loss is very low in these asymptomatic patients the mortality is still significantly higher as compared with patients without PAD (Figure 2). The most practical and reliable marker for estimating the prevalence of this disease is an ankle brachial index of less than 0.9[5]. Based on this criteria approximately 27 million people in Europe and North America are presumed to have PAD, with 8 to 12 million people in United States[3]. A study conducted in primary care offices in the United States demonstrated that approximately 30% of the patients greater than 70 years age or those greater than 50 years with history of smoking or diabetes mellitus, had PAD[6]. Another survey of French cardiologists showed that of their 100,429 patients, 10% had PAD. Intermittent claudication prevalence is much lower in younger age groups and increases dramatically with advancing age, ranging from 1% in those between ages of 55 to

Key words: Peripheral arterial disease, Intermittent claudication. Critical limb ischemia. Angiogenesis.

60 years to 4.6% in those between ages of 80 to 85 years[7].

The prevalence of PAD is particularly high in African American patients as compared with white or Hispanic populations and in patients with chronic renal failure[8]. Contrary to the earlier beliefs, prevalence of PAD is similar in women and men, however women may have more asymptomatic disease[9].



Criqui MH[1]

Figure 2:
Relative risk of death in 10 years in asymptomatic and symptomatic PAD as compared with normal

Source of data:
Criqui MH et al.[1]

Population studies have demonstrated that markers like soluble intercellular adhesion molecules - 1 (sICAM-1) and D-Dimer correlate significantly with the development of PAD[10], while as markers like hsCRP and D-Dimer have a strong association with poorer lower extremity functioning in PAD patients[11]. Factors recently reported to be associated with development of PAD are use of oral contraceptive agents[12] and depression[13].

The chronic occlusive arterial disease of the lower extremities is inseparable from the atherosclerotic disease of the other vascular beds including coronary and carotid arteries. Multivessel CAD is more frequently seen in those patients who have CAD in association with PAD as compared with patients who only have CAD[14]. Besides this approximately 22% of these patients will have 70% or greater carotid artery stenosis[15] and approximately 30% will have left ventricular systolic dysfunction[16]. These patients with PAD may be at an increased risk for ischemic cardiovascular events not only because of atherosclerosis in other vascular beds but also because of an enhanced pro-thrombotic state secondary to platelet activation[17-19].

A strong relationship has been noted with IL-6 gene polymorphism in patients with PAD suggesting that inflammation may be involved in pathogenesis.[20]. However no relationship was noted with ACE polymorphism[21] or V34L polymorphism[22, 23].

Poor Prognostic features: The following features correlate with increased incidence of future ischemic events in patients with PAD

1. ABI of less than 0.4[24].
2. Abnormal endothelium dependent flow mediated vasodilatation[25].
3. Elevated D-Dimer levels[26].
4. Low ADP induced platelet aggregation[26].
5. Prothrombin G20210A mutation[27].

DIAGNOSIS AND ASSESSMENT

The diagnosis of PAD begins with an accurate history, which should not only focus on symptoms referable to the lower extremity arterial beds but also to those originating in other vascular beds including the carotids, coronaries and renals. In patients who present with intermittent claudication non-vascular etiologies should be considered and differentiated from vascular ones.

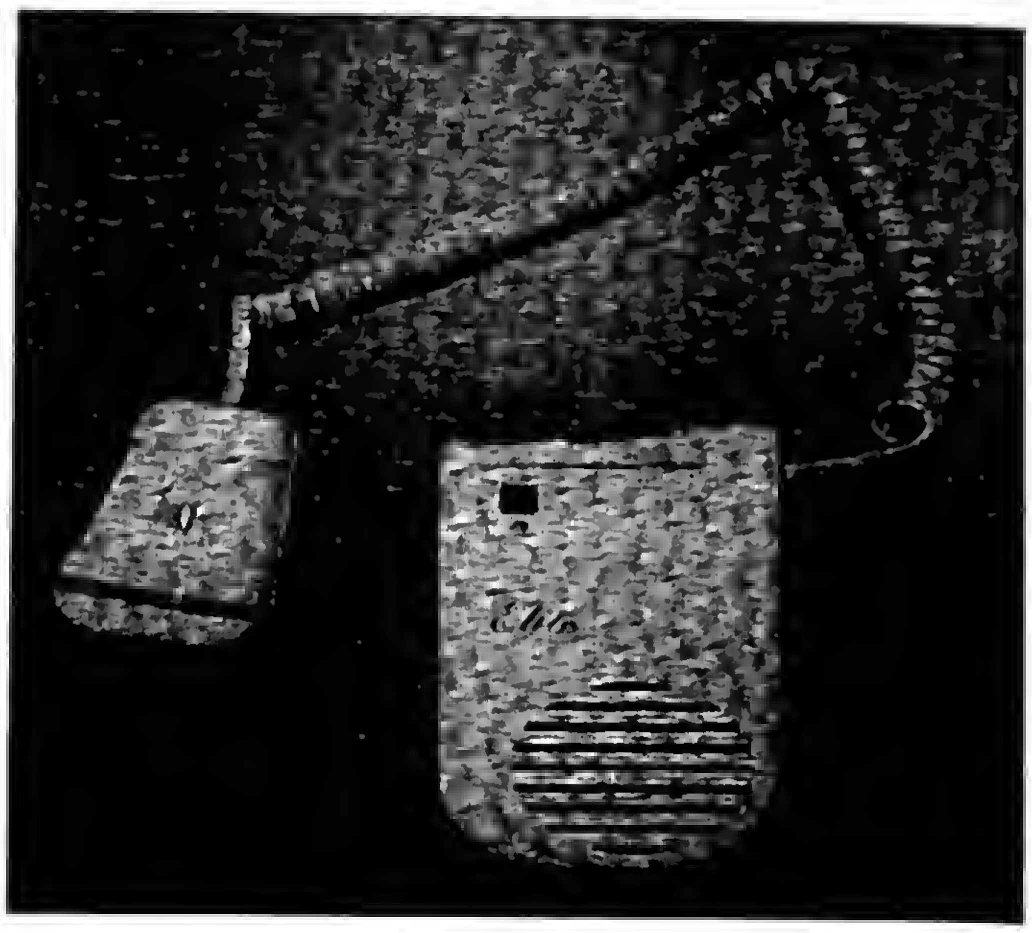


Figure 3 Picture of hand held Doppler

ANKLE BRACHIAL INDEX:

The most efficient, objective and practical means of documenting presence and severity of PAD is measurement of ankle brachial index. A resting ABI of less than 0.9 is considered abnormal and has a sensitivity of 95% and specificity of 100% for the detection of PAD, which is much better than several standard screening tests like pap smear, fecal occult blood or Mammography[3]. This test is useful in assessing the prognosis in both symptomatic and asymptomatic patients and its numerical valve has a very high correlation with mortality over 5 and 10 years[24]. ABI's also correlate highly with the severity of PAD disease with values between 0.5 to 0.9 usually seen in patients with claudication and less than 0.5 usually seen in patients with rest pain or tissue loss[28]. A small group of patients with normal ABI's and intermittent claudication should have exercise ABI to increase the sensitivity for detection of PAD. This is seen in patients with high-grade aorto-iliac stenosis or occlusion associated with large arterial collaterals. These patients with normal resting ABI's and abnormal exercise ABI's also have higher mortality as compared with patients with normal exercise ABI's. (M. Sheikh MD - Personal communication) Patients with diabetes mellitus and renal failure may have falsely elevated ABI's due to non-compressible and calcified lower extremity arteries. In these patients a toe brachial index (TBI) can be measured using a small toe cuff and PPG (Photoplethesmography). Transcutaneous oxygen (TcPO2) tension has also been used to assess the severity and response to various revascularization therapies especially in patients with CLI. Besides this TcPO2 is also useful in predicting the most appropriate level of amputation[29].

Although a thorough clinical examination is very useful in detecting the anatomical level of the disease, it is the segmental Doppler pressures, which objectively define the level of involvement.

DUPLEX ULTRASOUND:

Duplex ultrasound is also useful in assessing the patency of a previously treated arterial segment like a stented superficial femoral artery or a bypass graft. Although it may be useful in planning a percutaneous or a surgical revascularization, its utility in assessment of the entire lower extremity arterial system is highly imprecise despite the use of new ultrasound contrast-agents, which have improved its diagnostic ability for scanning difficult arterial segments.

MAGNETIC RESONANCE ANGIOGRAPHY & CT SCAN:

Comprehensive imaging of the peripheral vasculature has traditionally only been possible with catheter-based angiography. With the introduction of time of light magnetic resonance angiography (TOF MRA), non-invasive imaging of the peripheral arteries became a clinical reality and is being increasingly used in patients with PAD. Contrast enhanced MRA has higher sensitivity and specificity as compared with duplex ultrasonography and it approaches the accuracy of standard angiography. Its clinical utility using current technology has already been well established and the continued development of hard- and software will likely result in further performance improvements. Contrast enhanced MRA is likely to emerge as the dominant noninvasive imaging modality for PVD worldwide.

Multi-detector CT angiography also appears to be promising, with a recent study showing that when compared with digital subtraction angiography, CT angiography yielded a sensitivity of 91% and a specificity of 92% for lesions greater than 50%[31].

Fig 4: Ankle Brachial Index

$$ABI = \frac{\text{Systolic Ankle Pressure}}{\text{Systolic Brachial Pressure}}$$

Systolic Ankle Pressure is higher of the two Dorsalis pedis or Posterior tibialis systolic Pressures.

Systolic Brachial Pressure is the higher of the Brachial systolic Pressures.

THE RATIONALE FOR BEST MEDICAL TREATMENT

In these patients with PAD the risk of limb loss is much lower than the risk of death[28], which is mostly secondary to cardiovascular and cerebrovascular causes, hence these patients should be given "global vascular care" as opposed to "local care" only. The global care should involve the best medical care of atherosclerotic disease involving all vascular beds in addition to the local care in each vascular bed separately. The best medical care should encompass aggressive risk factor modification and anti-platelet therapy as described below.

Unfortunately physician from all specialties involved in the care of patients with PAD under-treat these patients. In a national physician survey it was clearly shown that atherosclerotic risk factor reduction and anti-platelet therapy was done much less frequently in PAD patients as compared with CAD patients. In the same study physicians perceived that antiplatelet therapy and cholesterol-lowering therapy were important more often for the CAD than for the PAD patient. Compared to other specialties, cardiologists had lowest thresholds, whereas vascular surgeons had the highest thresholds for initiating cholesterol-lowering interventions for the patient with PAD[12].

ANTIPLATELET AGENTS:

Antiplatelet agents should be considered as a cornerstone in the medical treatment of these patients with PAD. The consensus statement in 2003 has strongly recommended the use of antiplatelet agents in all patients with PAD, usually aspirin[13]. Although the CAPRIE study demonstrated a small incremental (8.7%) benefit of clopidogrel over aspirin in preventing stroke, myocardial infarction and vascular death in a prospectively stratified group of patients with PAD the cost effectiveness of this strategy needs further evaluation. One of the possible explanations for this added benefit might be that as many as 40% of PAD patients have an inadequate response to aspirin[14].

SMOKING CESSATION

Smoking is the most preventable cause of cardiovascular morbidity and mortality in patients with PAD. An epidemiologic study recently demonstrated the highest relative risk associated with PAD was current smoking with 32% of PAD being attributable to current smoking and 40% to past smoking. In contrast with its relationship to coronary disease and stroke, a history of previous smoking appears to have a persistent effect on the risk of PAD[15]. Hence all patients with PAD should be educated, encouraged and assisted in smoking cessation.

MANAGEMENT OF DIABETES MELLITUS

Intensive control of diabetes and Hemoglobin A_{1c} is recommended. Although there is no prospective data looking at diabetes control in patients with PAD, this position is supported by the previous studies suggesting lowered micro and macrovascular complications in patients with intensive control of diabetes and Hemoglobin A_{1c}[36, 37].

HYPERTENSION

The Framingham offspring study showed that hypertension and smoking were the two most important modifiable risk factors for PAD with odd ratio of 2.2 for hypertension and 2.0 for smoking[38]. Many studies have demonstrated that blood pressure control with anti-hypertensive agents leads to significant decrease in stroke, myocardial infarction, CHF, renal failure and death. This beneficial effect also extends to elderly patients with isolated systolic hypertension[39] and in patients with cardiovascular risk factors[40]. A recent study of 950 patients with PAD and type 2 diabetes mellitus showed that intensive control of blood pressure lowering to a mean of 127/75 mmHg resulted in marked reduction of cardiovascular ischemic events[41].

EXERCISE

All patients with PAD are advised to exercise regularly. Preferably they should join a supervised vascular rehabilitation program, which has been shown to be superior to home based exercise program[42]. Unfortunately because of little or no reimbursement, supervised PAD rehabilitation is not widely available. This may change in near future with the publication in the United States of a CPT code (93668) by the American Medical Association. Many patients with symptomatic PAD may not be able to exercise optimally because of claudication and hence they adopt a relatively sedentary life style. This leads to a worsening of their cardiovascular risk profile and a higher risk of cardiovascular events, which is the major cause of increased mortality. This risk profile can be remarkably improved with supervised vascular rehabilitation, which has been shown to improve peak walking distance and pain free walking distance by 100% or greater[43].

Recent studies have shown that improvements in walking abilities after 6 months of exercise rehabilitation are sustained for an additional 12 months in older patients with intermittent claudication using a less frequent exercise maintenance program[44]. Besides this, a short-course training program was also noted to enhance the walking ability in patients with moderate-to-severe intermittent claudication[45].

REDUCTION IN CHOLESTEROL

The ATP III guidelines clearly delineate goals for lipid lowering in patients with PAD. However, several reports in last few years have demonstrated that greater than 50% of patients with PAD treated by primary care physicians[2], vascular surgeons[46] and endovascular specialists[47], have their lipid levels above the NCEP goals. This importance of this was highlighted by a study from suburban New York which showed that patients with PAD and no CAD had higher coronary events if they were not treated with statins than patients with CAD and PAD who received lipid lowering therapy[48].

Besides preventing cardiovascular events statins have been shown improve pain free walking distance and other leg functioning parameters in patients with PAD. Hence they may also have a favorable effect on the lifestyle[49, 50].

PHARMACOTHERAPY.

Cilostazol - a phosphodiesterase III inhibitor with antiplatelet and vasodilatory properties, is a promising drug available to treat patients with intermittent claudication. A recently published meta-analysis of six trials has shown that treatment with cilostazol was associated with greater improvements in community-based walking ability and health related quality of life in patients with intermittent claudication than treatment with placebo[51]. Clinical studies have also demonstrated that cilostazol favorably alters plasma lipid profile by elevating HDL-cholesterol and lowering triglycerides[52]. Several other agents that have been shown to benefit intermittent claudication include pentoxyphylline, naftidrofuryl, oral heparan sulfate, and intravenous glutathione infusion, however the use of all these agents in clinical setting is still controversial.

Patients with critical limb ischemia are best served by endovascular or surgical revascularization, however patients who are not good candidates for revascularization may benefit from long term intermittent use of prostanoids including prostaglandin E1, iloprost, and Treprostinil[53]. These agents reduce rest pain and ulcer size, however the benefit of these agents in intermittent claudication is still controversial[54]. Hyperbaric oxygen, artificial CO_2 foot bathing and intermittent pneumatic compression devices have also shown promise in healing of the CLI patients with ulceration or gangrene[55, 56].

In patients primarily considered for surgical treatment, antiplatelet and anticoagulant drug therapy can be used as a means of promoting graft patency, and beta-adrenergic blockers can be used as a means of reducing the peri-operative risks associated with vascular surgery.

PERCUTANEOUS AND SURGICAL REVASCULARIZATIONS.

In general, a comparison of techniques for revascularization demonstrates similar initial technical success rates for surgery and percutaneous transluminal angioplasty. Angioplasty is often associated with lower procedural morbidity and mortality rates. Conversely, surgery frequently provides greater long-term patency, however late failure of percutaneous therapies may often be treated successfully with re-intervention. Additionally a combined or a hybrid revascularization procedures have also been gaining popularity especially amongst the surgical community[57].

The last decade has seen an explosive growth of endovascular technologies, most of which have found an application in the treatment of PAD.

A recent study suggested the safety and efficacy of abciximab as an adjunct during complex infrainguinal arterial interventions[58]. The endovascular treatment of long SFA lesions or occlusions has seen a significant progress with several reports demonstrating that subintimal angioplasty is feasible and effective in revascularization of these patients[59-60]. Endovascular brachytherapy (EVBT) has also been noted to improve the patency of femoro-popliteal arteries undergoing PTA in the short-term, particularly in non-diabetics with long occlusions[61]. However late thrombotic occlusion following EVBT is still a concern even in PAD interventions[62]. The introduction of drug eluting stents(DES) in the treatment of SFA disease has a great potential for the prevention of in-stent restenosis, at least in the short term follow-up[63]. If the results of DES are as good as they have been in the coronary circulation than endovascular treatment of SFA occlusions may be accepted as a first line therapy for these patients. Endovascular treatment of infra-renal aortic stenosis/occlusion and aorto-iliac stenosis/occlusions was also reported to be highly successful and had a greater than 85% primary patency rate at 36 months[64].

In patients with critical limb ischemia endovascular treatment including PTA of the infra-popliteal vessels was reported to be feasible and an effective form of revascularization. Clinical recurrences were infrequent and the procedure could successfully be repeated in most cases. In subjects treated successfully with PTA the above-the-ankle amputation rate was low[65].

In patients with acute limb ischemia reports about the use of TNK-tPa for catheter-directed thrombolysis demonstrated that it produced marked improvement or complete resolution in more than 87% of patients with a reasonable safety profile[66]. Besides this in a small number of patients combination thrombolysis using full dose glycoprotein IIb/IIIa receptor antagonist and low dose reteplase was reported to be effective in treatment of acute femoropopliteal thrombosis[67].

Several newer devices, catheters, balloons and stents have been developed some of which are already in the market and some of which are in clinical trials. For example a 6 mm cutting balloon has been shown to be useful in lesions resistant to conventional angioplasty[68], while PTFE-covered nitinol stents were demonstrated to have an acceptable safety profile and were effective from a short-term perspective in femoropopliteal interventions[69].

THERAPEUTIC ANGIOGENESIS:

This process of improving collateral vessel development holds a significant promise in patients with coronary and peripheral arterial disease. The two methods to induce angiogenesis are use of angiogenic growth factors or bone marrow mononuclear cell therapy. The benefit of using growth factor therapy with Fibroblast Growth Factor (FGF) and vascular endothelial growth factor (VEGF) - adenovirus mediated gene transfer in patients with intermittent claudication, is still controversial[70, 71]. However in patients with CLI gene transfer using naked plasmid DNA encoding for VEGF and bone marrow mononuclear cell therapy demonstrated significant improvement in tissue loss, resolution of rest pain and lowering the level of amputation[72-73]. Currently there are several controlled studies evaluating the potential role of inducing angiogenesis in these critical limb ischemia patients with hepatocyte growth factor (HGF), VEGF and FGF. The other major area is the prevention of graft disease and restenosis using antisense oligodeoxynucleotides.

SUMMARY

PAD is being increasingly identified, due to better diagnostic testing, and the increasing prevalence in our aging population. Despite this, there remains substantial percentage of patients who are not diagnosed with this disorder and this is seen in all types of health care settings. Hence these patients continue to have increased morbidity and mortality, largely due to progressive atherosclerosis in multiple vascular beds. Whereas surgical, endovascular and medical therapies for atherosclerosis in general, and PAD in specific, continue to develop, there appears to be considerable room for improvement in physician adoption of proven effective therapies such as cholesterol lowering therapies and blood pressure management. Additionally, new therapies, such as gene transfer and cell therapy, are under development for this population.

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JK-PRACTITIONER

THE IMPACT OF DIABETES ON THE CARDIOVASCULAR SYSTEM AND MANAGEMENT STRATEGIES

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By the year 2020. type 2 diabetes will overtake infectious diseases as the biggest killer world-wide. Recent estimates suggest that there are presently 200 million people with type 2 diabetes with the numbers set to increase to 300 million over the next two decades[1]. This is partly due to the ageing population, but also the increasing prevalence of obesity and sedentary lifestyle particularly of Asian extraction where prevalence of type 2 diabetes rates are four times those seen in the indigenous white Caucasian population.

Patients with type 2 diabetes have a significantly increased risk of developing cardiovascular disease. Once clinical cardiovascular disease develops. these patients have a poorer prognosis than normoglycemic patients. By inducing endothelial changes. hyperglycemia contributes directly to atherosclerosis. Type 2 diabetes is also associated with atherogenic dyslipidemias. This form of diabetes, or the precursor state of insulin resistance, commonly occurs as a metabolic syndrome (formerly known as syndrome X) consisting of hypertension, atherogenic dyslipidemia and a procoagulant state, in addition to the disorder of glucose metabolism. All cardiovascular risk factors except smoking are more prevalent in patients with type 2 diabetes[2].

ATHEROGENIC MECHANISMS IN DIABETES

Links between endothelial dysfunction, atherosclerosis and diabetes have been increasingly recognized. One of the earliest discernible atherogenic changes in diabetes is endothelial dysfunction, which is characterized by abnormal endothelium-dependent vasodilation, where it may contribute to ischemia and its sequelae by inhibited vasodilation, vascular smooth-muscle proliferation, increased thrombogenesis and proatherogenic cellular processes[1]. Hyperglycemia and atherosclerosis in type 2 diabetes are related. Hyperglycemia causes glycosylation of virtually all proteins, inducing collagen cross-linking with other extracellular matrix proteins in the arterial wall[4]. Long-term exposure to elevated glucose levels alone can cause the endothelial cell dysfunction observed in diabetes. Accelerated atherosclerosis, thrombosis, hypertension and hyperlipidemia all participate in the pathogenesis of vascular disease in patients with diabetes, and endothelial dysfunction is probably involved in each of these vascular abnormalities[5].

METABOLIC SYNDROME

Atherogenic dyslipidemia is often associated with other risk factors for coronary heart disease. This constellation of risk factors, evolved from older concepts of syndrome X and the insulin resistance syndrome, has been termed the "metabolic syndrome" (Table 1)[6]. It is not essential for all elements of this syndrome to be present in a single patient. The metabolic syndrome of atherogenic dyslipidemia, hypertension, insulin resistance with or without type 2 diabetes, and the procoagulant state is commonly associated with truncal obesity and hyperuricemia. Together, hypertension and overt diabetes double the risk of cardiovascular disease[7].

Truncal obesity, a prominent feature of the metabolic syndrome8 , frequently observed in patients with type 2 diabetes, is virtually always accompanied by insulin resistance[9]. The distribution of fat, rather than overall obesity, determines risk. The reported association between increased abdominal (upper body) fat and an increased risk of coronary heart disease relates to visceral fat, for which the waist-to-hip ratio is a convenient index. A waist-to-hip ratio of greater than 1.0 in men and 0.8 in women indicates abdominal obesity[10]. The waist circumference alone also correlates well with the amount of visceral fat, and the

Key words: Meningins. Tuberculosis. Hydrocephalus

relationship is similar in men and women[11]. Increased concentrations of plasminogen activator inhibitor 1 are associated with deficient fibrinolysis[12]. In addition, the 16-year follow-up of the First National Health and Nutrition Examination Survey suggests that hyperuricemia is significantly and independently associated with the risk of cardiovascular mortality[13].

HYPERHOMOCYSTEINEMIA

Hyperhomocysteinemia has recently been recognized as an independent risk factor for cardiovascular disease. This condition has an estimated prevalence of 5 to 30 percent in the general population[14]. A large-scale prospective study found that the five-year mortality risk was almost two times higher in patients with hyperhomocysteinemia and type 2 diabetes than in patients with hyperhomocysteinemia but no diabetes[14]. A recent meta-analysis found that folic acid in a dosage of 0.5 to 5 mg per day can lower serum total homocysteine levels by 15 to 40 percent within about six weeks[15]. However, no interventional evidence has related blood levels of homocysteine reduced by folic acid to reduced rates of cardiovascular disease in controlled trials. Therefore, attention should not be diverted from traditional risk-lowering strategies in favor of folic acid supplementation[16].

The cardiovascular complications of diabetes which require special consideration include :

- Dyslipidemias
- Hypertension
- Left ventricular dysfunction-both systolic and diastolic
- Heart failure
- Acute Coronary Syndromes (angina, MI)

Atherosclerosis is accelerated in patients with diabetes, and the development of coronary heart disease worsens the prognosis[17]. With the exception of smoking, all potentially reversible risk factors for coronary heart disease are more prevalent in patients with diabetes than in the general population. Because one half of patients with type 2 diabetes already have evidence of coronary heart disease at the time their diabetes is diagnosed,[18] the distinction between primary prevention in high-risk patients and secondary prevention in those with clinical coronary heart disease may be arbitrary in patients with diabetes[17].

ATTENUATING RISK FACTORS FOR CORONARY HEART DISEASE IN TYPE 2 DIABETES

Based on the results of clinical trials in patients with and without diabetes, the American Diabetes Association (ADA) has issued treatment goals and guidelines for managing dyslipidemia (Table 3)[19]. New recommendations on nutrition[20] and exercise[21] have also been published.

DIET AND EXERCISE

Dietary modification and increased physical activity are the mainstays of nonpharmacologic treatment[22]. The American Heart Association's step I and step II diets emphasize the consumption of foods that are low in fat (especially saturated fat) and cholesterol and reducing the intake of 'red' meat. Weight loss can improve glucose control and reduce lipid levels. Weight loss seems preferentially to reduce atherogenic visceral fat, and the resultant metabolic improvement appears to be disproportionately greater than the amount of weight lost[23]. Today there is no one prescribed "diabetic" or ADA diet. Current ADA guidelines for medical nutrition therapy stress the use of an individual approach, preferably in consultation with a registered dietitian and with consideration given to the patient's usual eating habits and lifestyle[20]. The diet should be geared toward achieving treatment goals for glucose control, lipid levels and blood pressure, as well as maintaining reasonable weight and adequate nutrition. No matter what the patient's starting weight is, moderate weight loss (4.5 to 9.1 kg [10 to 20 lb]) has been shown to reduce hyperglycemia, dyslipidemia and hypertension[24]. New diet related treatments include Orlistat, a pancreatic lipase inhibitor which reduce the efficiency of fat absorption and causes significant weight reduction. Other similar options not yet fully explored include alpha-amylase inhibitors.

Table 1 : Metabolic Syndrome

Component Risk Factor	Contributing Causes
Atherogenic Dyslipidemia	Obesity (especially central)
Hypertension	Sedentary lifestyle
Insulin Resistance with or without Type 2 diabetes	Cholesterol raising nutrients
Procoagulant state	Ageing, Genetic factors

Table 2 : Risk Factors for Cardiovascular Disease in Patients with Diabetes

Modifiable	Non Modifiable
Cigarette smoking	Genetic factors
Hypercholesterolemia	Family History
Albuminuria	Disease duration
Hyperinsulinemia	Patient's age and sex
Hypertension	
Low HDL cholesterol levels	
Hyperglycemia	
Obesity	

Table 3 :
Lipoprotein Risk Factors For Coronary Heart Disease in Type 2 diabetes

Lipoprotein	optimal level, mg/dl (mmol/l)	Risk levels, mg/dl(mmol/l) low	borderline	high
LDL cholesterol	<100 (2.60)	<100	100 to129(2.60 to 3.34)	130(3.35)
HDL cholesterol	>45 (1.15)	> 45	33 to 45 (0.85 to 1.15)	<35(0.90)
Triglycerides	<200(2.26)	<200	200 to 399(2.26 to 4.50)	400(4.52)

Similarly, exercise can substantially improve the metabolic abnormalities in type 2 diabetes. An exercise program is most

Table 4 :
Priorities for the Treatment of Dyslipidemia in Adult Patients with Diabetes

Priorities in descending order of importance	Goal level, mg per dL (mmol per L)	Therapy
Lower LDL cholesterol levels.	<100(2.60) in patients with CHD <130 (3.35) in patients without CHD	Statin (HMG-C0A reductase inhibitor); sequestrant (binding resin) added if needed
Raise HDL cholesterol levels.	>45(1.15)	Behavioral interventions; glycemic control Difficult to increase HDL cholesterol level except with nicotinic acid.
Lower triglyceride levels	<200 (2.26)	Glycemic control; fibric acid derivative (fibrate); statin in patients who also have high LDL cholesterol levels*
Treat combined hyperlipidemia	Same as above	Improved glycemic control and one of the following: a statin; a statin and a fibrate*; a binding resin and a fibrate; a statin and nicotinic acid.*.

*The combination of a statin with nicotinic acid and especially with a fibrate may carry an increased risk of myositis.

effective when it is instituted early in the disease process. Benefits include an improved lipoprotein profile, reduced blood pressure and increased cardiovascular fitness[25]. Exercise may also enhance weight loss, and a disproportionate effect of exercise on abdominal fat has been reported[26]. The specific recommended program will depend on the evidence of cardiovascular disease.

SMOKING CESSATION

Cigarette smoking doubles the risk of cardiovascular disease in patients with diabetes and attenuates whatever benefits accrue from modifying other risk factors[5]. The Multiple Risk Factor Intervention Trial (MRFIT) quantified an independent and increasing risk of coronary heart disease mortality based on the number of cigarettes smoked per day[26]. Cigarette smoking appears to act synergistically with hypercholesterolemia, possibly by enhancing the oxidation of LDL cholesterol[27]. Weight gain is a real concern for those who quit smoking using nicotine replacement therapy. Physicians should inform patients of this potential and reaffirm the health benefits of cessation.

ANTIOXIDANT THERAPY

Given the current focus on lipid oxidation in the pathogenesis of atherosclerosis, the increase in oxidized LDL cholesterol found in patients with diabetes would seem to provide a rationale for antioxidant therapy[28]. Observational and epidemiologic studies have suggested that persons and populations with high plasma levels of vitamin E have lower rates of coronary heart disease, and an inverse relationship has been found between b-carotene and cardiovascular mortality[29]. A prospective study of high doses of vitamin E from natural sources, however, led to the conclusion that vitamin E had no demonstrable effect on cardiovascular outcomes in a high-risk population followed for four to six years[30]. Current opinion is that dietary antioxidants are strongly recommended.

LDL CHOLESTEROL TARGET LEVELS

Current ADA guidelines accord lowering LDL cholesterol levels the highest treatment priority, followed by raising HDL cholesterol levels and lowering triglyceride levels (Table 4)[29] LDL cholesterol levels in patients with type 2 diabetes may be similar to those in normoglycemic patients, but the composition of the particles (smaller and denser) may make them more atherogenic.

STATINS

Statins are the first-line agents for use in reaching target LDL cholesterol levels, with a bile acid sequestrant (binding resin) added if needed[18]. After four to eight weeks of therapy, statins generally reduce LDL cholesterol levels by 20 to 60 percent, which can also favorably affect triglyceride levels.[18,19,31] In patients with triglyceride levels in the range of 200 to 250 mg per dL (2.26 to 2.82 mmol per L), the percent reduction in the triglyceride levels will equal the reduction in the LDL cholesterol level.[32] Statins lower VLDL cholesterol levels as well as LDL cholesterol levels; benefits in patients with diabetes may relate to the combined activity.[32 33]

The rationale for considering the LDL cholesterol level as the primary lipoprotein level to modify is based on the results of recent long-term clinical trials such as the Scandinavian Simvastatin Survival Study (4S)[34] where the risk of major coronary events in patients with diabetes was reduced by 35 percent, and the risk of any atherosclerotic event was reduced by 37 percent. Total mortality in patients with diabetes was reduced by 43 percent; and the Cholesterol and Recurrent Events (CARE) trial[34] where the risk of major coronary events was reduced by 25 percent in patients with diabetes.

BILE ACID SEQUESTRANTS

Bile acid sequestrants are effective in decreasing LDL cholesterol and total cholesterol levels, but they may worsen hypertriglyceridemia.[7] Long-term use appears to be safe, and these agents are particularly useful for treating younger patients and women who are considering pregnancy.[35] Because bile acid sequestrants can elevate VLDL cholesterol and triglyceride levels, they are a questionable choice for monotherapy in patients with type 2 diabetes.[35]

FIBRIC ACID DERIVATIVES

Fibric acid derivatives, often termed "fibrates," reduce VLDL cholesterol and triglyceride levels, increase HDL cholesterol levels and have variable effects on LDL cholesterol levels.[35] In the Veterans Affairs Cooperative Studies Program High-Density Lipoprotein Cholesterol Intervention Trial (VAHIT),[36] gemfibrozil increased HDL cholesterol levels and decreased triglyceride levels in men with and without diabetes who had coronary heart disease and low HDL cholesterol levels as the primary lipid abnormality. After five years, VAHIT investigators found that the risk of a major coronary event was 22 percent lower and the risk of the combined outcome of coronary heart disease death, nonfatal myocardial infarction or stroke was 24 percent lower in gemfibrozil-treated patients compared with placebo-treated patients. In patients with extremely high triglyceride levels, gemfibrozil may elevate LDL cholesterol levels as it lowers triglyceride levels.[4,12]

NICOTINIC ACID

When given in dosages well above those needed for the vitamin requirement, nicotinic acid favorably affects all lipids and lipoproteins. It also raises HDL cholesterol levels. The high frequency of side effects associated with nicotinic acid is a major disadvantage; flushing, which results from vasodilation, is particularly troublesome, although aspirin or other prostaglandin synthesis inhibitors can decrease this adverse effect.[12] Because nicotinic acid is associated with hyperglycemia and possibly increases insulin resistance, many authorities do not use this agent in patients with type 2 diabetes.[4]

ANTIHYPERTENSIVE DRUG THERAPY

Control of hypertension is a cornerstone of treatment to prevent cardiovascular complications in patients with diabetes. The risk of these complications is lowest in adult patients whose average blood pressure is less than 120/80 mm Hg, with the risk of complications increasing exponentially as blood pressure increases. In patients with diabetes, the threshold for instituting medical therapy is a blood pressure of 130/85 mm Hg.[17]

Tight control of blood pressure has been shown to reduce cardiovascular morbidity and mortality in patients with diabetes. Because of efficacy and a low incidence of side effects, angiotensin-converting enzyme (ACE) inhibitors are a reasonable first choice in patients with diabetes, hypertension and albuminuria. ACE inhibitors, alpha blockers, calcium channel blockers and low-dose diuretics have relatively few adverse effects on glucose homeostasis, lipid profiles and renal function.[17]

The benefits of ramipril were observed among patients who were already taking a number of effective treatments, such as aspirin, beta-blockers, and lipid-lowering agents, indicating that the inhibition of angiotensin-converting enzyme offers an additional approach to the prevention of atherothrombotic complications. A reduction of 2 mm Hg in diastolic blood pressure might at best account for about 40 percent of the reduction in the rate of stroke and about one quarter of the reduction in the rate of myocardial infarction.[18] However, the results of recent studies, such as the Hypertension Optimal Treatment study,[39] suggest that for high-risk patients (e.g., those with diabetes), it may be beneficial to lower blood pressure even if it is already within the "normal" range. Moreover, a recent reanalysis of 20 years of blood-pressure data from the Framingham Heart Study[40] suggests that the degree of benefit expected from a decrease in blood pressure may have been underestimated. Despite these considerations, it is likely that angiotensin-converting-enzyme inhibitors exert additional direct mechanisms on the heart or the vasculature that are important. These may include antagonizing the direct effects of angiotensin II on vasoconstriction,41 the proliferation of vascular smooth-muscle cells,[41] and rupture of plaques[42]; improving vascular endothelial function41; reducing left ventricular hypertrophy; and enhancing fibrinolysis.[41] Ramipril is beneficial in a broad range of patients without evidence of left ventricular systolic dysfunction or heart failure who are at high risk for cardiovascular events. Treatment with ramipril reduced the rates of death, myocardial infarction, stroke, coronary revascularization, cardiac arrest, and heart failure as well as the risk of complications related to diabetes and of diabetes itself. These effects may be mediated by improved insulin sensitivity, a decrease in hepatic clearance of insulin, an antiinflammatory effect, improved blood flow to the pancreas,[43] or an effect on abdominal fat.[44] The results are also consistent with the results of the recent Captopril Prevention Project study,[45] which indicated a lower rate of newly diagnosed diabetes in patients who were randomly assigned to receive captopril than in those who were assigned to receive a diuretic or beta-blocker. These findings clearly demonstrate that ramipril, a long-acting angiotensin-converting-enzyme inhibitor, reduces the rates of death, myocardial infarction, stroke, revascularization, cardiac arrest, heart failure, complications related to diabetes, and new cases of diabetes in a broad spectrum of high-risk patients.

DIABETES AND LEFT VENTRICULAR DYSFUNCTION

There are a number of unresolved issues concerning the relation between diabetes and left ventricular (LV) dysfunction that result in ongoing uncertainties regarding the management of the diabetic patient with heart failure. It is clear that diabetes predisposes to impaired LV systolic and diastolic function. However, it is often difficult to ascertain whether the impact of diabetes on LV function represents specific, direct metabolic effects on the myocardium or merely the effects of concomitant CHD or hypertension, which are common comorbid conditions in patients with diabetes.

MECHANISMS RESPONSIBLE FOR LV DYSFUNCTION IN DIABETES

The mechanisms by which diabetes predisposes to LV dysfunction and heart failure include (1) concomitant CHD, (2) concomitant hypertension, (3) LV hypertrophy, (4) disease of the coronary microvasculature, (5) endothelial dysfunction, (6) obesity, (7) autonomic dysfunction, and (8) metabolic abnormalities that contribute to the diabetic cardiomyopathy. Endothelial dysfunction is a characteristic of diabetes, and endothelium-derived substances may have profound effects on myocardial structure and function. For example, both endothelin and angiotensin II cause myocardial hypertrophy and increased interstitial connective tissue, and both may also contribute to myocardial apoptosis. Obesity, an integral component of the metabolic syndrome and type 2 diabetes, predisposes to the toxic effects of fatty acids on the myocardium and the additional detrimental effects of cytokines and angiotensin II released by adipose tissue. The possibility of a specific diabetic cardiomyopathy has been the subject of debate for decades, but there are now substantive data indicating that diabetes impairs LV function through direct and indirect mechanisms. Several experimental models of diabetes have demonstrated altered myocyte gene expression, disorders of calcium ion homeostasis, and abnormal systolic and diastolic function in relation to elevations of blood glucose.46 It is also evident from natural history studies that the early cardiovascular manifestations of diabetes include increased LV mass and hyperdynamic LV function that may be related to a hyperadrenergic state.[47] Such effects may also contribute to myocardial apoptosis and increased interstitial connective tissue deposition. Persons with diabetes and hypertension have greater LV mass and wall thickness than nondiabetic hypertensive patients.[48]

Diabetes and Onset of Heart Failure With Normal Systolic Function

It is a well-known clinical observation that heart failure symptoms can develop in patients with normal LV systolic function, and when this occurs, diabetes is often a contributing factor. The pathophysiology, management, and outcomes of persons with diabetes, heart failure, and preserved systolic function have not been specifically addressed. Management strategies are generally those recommended for LV systolic dysfunction, including use of ß-blockers and ACEIs, although there is a paucity of data supporting such practice.

DIABETES AND ONSET OF LV SYSTOLIC DYSFUNCTION

Several longitudinal community-based studies have identified diabetes as a major risk factor for development of clinical heart failure. The Framingham Study, demonstrated nearly 2 decades ago that patients with diabetes have a greater likelihood of developing clinical heart failure.[49] The Framingham experience has been confirmed in several recent smaller series. In the Glasgow MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) cohort,[50] the frequency of LV systolic dysfunction was highest in persons with diabetes. In the New Haven cohort of the Established Population for Epidemiologic Studies of the Elderly,[51] diabetes was the strongest predictor of development of heart failure. Similarly, in the Cardiovascular Health Study, diabetes doubled the risk of developing heart failure in men over the course of 5.5 years and tripled the risk in women.[52] Finally, recent data from the Kaiser Health System[53] have demonstrated that diabetes control also significantly affects the likelihood of developing heart failure. In patients with Hb A1c <7%, the rate of heart failure was 4.2 per 1000 per year; in patients with Hb A1c >10%, this rate increased to 9.2 per 1000 per year.[53] This effect was more pronounced in men than in women.

It is probable that the majority of persons with diabetes and heart failure in the multicenter heart failure trials are also those with CHD, with the expected worse prognosis of coronary disease patients with LV dysfunction. However, even among patients with CHD and LV dysfunction, those with diabetes have a higher mortality than those without diabetes, as reported in a retrospective analysis of the Studies of Left Ventricular Dysfunction (SOLVD) database.[54] No other multicenter trial or registry has described the diabetic populations regarding presence of underlying coronary artery disease, and no study (including the SOLVD database) has evaluated severity of CHD in the diabetic population relative to the nondiabetic population. In addition, no trial has described the diabetic patients with reference to hypertension and hypertension control. The available data do uniformly demonstrate that persons with diabetes and heart failure represent a very-high-risk group with a substantially worse prognosis than those without diabetes.

The SOLVD Treatment and Prevention Trials[55] and the Trandolapril Cardiac Evaluation (TRACE) trial[56] reported the effects of ACEI therapy on outcome of persons with diabetes and heart failure. In the 3 trials, mortality and heart failure hospitalization rates were higher in patients with diabetes than in persons without diabetes. In the SOLVD Treatment Trial, enalapril provided no significant mortality reduction in patients with diabetes, whereas there was a significant reduction in mortality in such patients receiving enalapril in the SOLVD Prevention Trial and in those receiving trandolapril in the TRACE trial.

Only one of the trials investigating ß-blocker therapy in heart failure examined the effect of such therapy in patients with diabetes. MERIT-HF (Metoprolol Controlled-Release Randomised Intervention Trial in Heart Failure)[57] demonstrated that patients with diabetes had higher mortality than heart failure patients without diabetes. However, a subset analysis failed to demonstrate a significant survival benefit in patients with diabetes after ß-blocker therapy with metoprolol. Whether this represents the effects of a ß1-selective agent and whether greater efficacy may be achieved in patients with diabetes with use of a nonselective ß-blocker with 1-blocking properties, such as carvedilol,[58] will be determined only by future trials or analysis of existing trial data.

ACUTE MYOCARDIAL INFARCTION

In-hospital and long-term mortality rates after acute myocardial infarction (AMI) are twice as high among individuals with diabetes as among those without diabetes[59,60]. Diabetes is also a major risk factor for adverse outcomes in patients with unstable angina. Risk of first myocardial infarction often exceeds 3% whereas risk of recurrent myocardial infarction may be 7% per annum or greater in people with type 2 diabetes. Although 3% per annum is the advocated (and accepted) threshold for intervention with lipid lowering therapy to reduce risk, most people with diabetes are currently not treated. Evidence from large prospective epidemiology studies conducted in individuals predominantly not known to have diabetes shows that people with increased ratios of low density lipoprotein cholesterol (LDLc) to HDLc in combination with increased plasma triglyceride levels markedly increases risk of myocardial infarction. It is this lipid abnormality that occurs in people with insulin resistance, the metabolic syndrome and/or type 2 diabetes. Many individuals with plasma glucose concentrations close to the upper limit of the normal range have features of the metabolic syndrome contributing to a marked increase in risk of atherovascular disease (AVD). Although there is evidence of effectiveness, both clinical and cost-effectiveness, to support the use of thrombolytics, beta-blockers, ACE inhibitors, lipid lowering agents and aspirin in people with established AVD, there is limited evidence to date to support their use in primary prevention. Since absolute risk of a first myocardial infarction in many people with diabetes is similar to risk of a recurrent myocardial infarction in individuals with normal glucose tolerance, interventions normally used in secondary prevention should be considered for primary prevention in many patients with type 2 diabetes.

There are numerous factors responsible for this increased risk. Thrombolytic trials have demonstrated improved outcomes with reduction in the time to presentation and to institution of treatment. Persons with diabetes, particularly in the setting of autonomic neuropathy, have impaired angina recognition and may not consider shortness of breath, nausea, vomiting, unexplained fatigue or diaphoresis, or disturbances of glycemic control as symptoms of cardiac ischemia[61]. Too often, AMI is the first clinical expression of CHD in the patient with diabetes, who may have experienced prior, unheeded symptoms of cardiac ischemia. Furthermore, one should not assume that the absence of angina in the post-myocardial infarction (MI) patient is a reliable index of CHD stability.

Factors specific to diabetes may not only increase the risk of MI62 but also adversely affect its outcome. Autonomic nervous system (ANS) dysfunction results in sympathovagal imbalance and may lower the threshold for life-threatening arrhythmia and increase the risk of hemodynamic instability. Up to 50% of individuals with type 2 diabetes (with disease duration >10 years) have ANS dysfunction manifested as impaired heart rate variability. Fibrinogen levels may be elevated in patients with diabetes, particularly in the setting of proteinuria or poor glycemic control. Elevated levels of plasminogen activator inhibitor-1 indicate impaired fibrinolysis, and diabetic platelets are more aggregable than nondiabetic platelets. Such diabetes-related alterations may increase the risk of thrombosis at the site of plaque disruption and possibly increase the risk of reinfarction after thrombolytic therapy. The diabetic ventricle is more prone to maladaptive remodeling, which increases the risk of heart failure and cardiogenic shock. The status of the noninfarct zone, an important determinant of the remodeling process, may be affected by silent infarction, ANS-related diastolic or systolic dysfunction, diabetic or hypertensive cardiomyopathy, impaired microvascular perfusion, and more extensive epicardial CHD[64].

AMI patients with diabetes are distinguished by a higher prevalence of comorbidities, including dyslipidemia, hypertension, renal insufficiency, and peripheral and cerebral vascular disease. There is a higher rate of previous MI, an excess risk of heart failure before and at presentation, and more extensive epicardial CHD. Patients with diabetes present at a younger age; women are affected as often as men.

In almost all respects, the management of AMI is similar for patients with and without diabetes[64]. Substantial evidence points to the admission glucose level as an independent predictor of early and late mortality after MI in patients with and without diabetes.65 The DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) study suggests that strict glycemic control for 3 months can significantly improve survival at 1 and 3 years after MI[66].

Targets for treatment include reestablishment of coronary flow and myocardial perfusion, plaque stabilization, prevention of recurrent ischemia, limitation of LV remodeling, arrhythmia suppression, and initiation of a lifelong program of secondary prevention.

REPERFUSION THERAPY

There are very limited data regarding the impact of myocardial revascularization on survival and quality of life in patients with diabetes, CHD, and LV dysfunction. A retrospective analysis of data from the SOLVD Treatment and Prevention Trials has demonstrated a significant improvement in survival in such patients with myocardial revascularization plus medical therapy and also an improvement in symptoms and reduction in hospitalization for heart failure.

Persons with diabetes derive the same or greater relative survival benefit from fibrinolytic therapy as those without diabetes[67]. Previous concerns about the hemorrhagic risk associated with diabetic retinopathy have not been substantiated. Similarly, acute success rates with primary percutaneous coronary intervention are comparable in the presence or absence of diabetes, although restenosis and long-term mortality rates remain higher in patients with diabetes[68,69]. The Bypass Angioplasty Revascularisation Trial (BARI) suggested that coronary artery by-pass surgery was a better means of revascularisation than angioplasty with only 66% of randomised patients surviving 5 years following angioplasty compared with 81% of patients who had coronary artery surgery. The widespread use of coronary stents and the adjunctive use of platelet Ib/IIIa inhibitors have greatly reduced the complications and restenosis rates following angioplasty. The EPISTENT trial has shown that the use of the platelet inhibitor abciximab in coronary angioplasty reduces the risk in a diabetic patient to that of a non-diabetic patient.

It has been demonstrated that in cases of triple or diffuse vessel disease, stent placement is associated with a higher rate of restenoses as compared to non diabetic populations. CABG is a better option. Of the OHAs , rosiglitazone has shown to be of benefit in retarding the rate of fibrosis in cases where stenting has been opted for.70

ANTIPLATELET THERAPY

The American Diabetes Association Position

Statement on Aspirin in Diabetes, 2001, made the following recommendations:

- A family history of coronary heart disease
- Cigarette smoking
- Hypertension
- Obesity (>120% desirable weight) or BMI >27.3 in women, >27.8 in men
- Albuminuria (micro or macro)
- Lipids:
  - o Cholesterol >5.2mmol/L
  - o LDL cholesterol >2.6mmol/L
  - o HDL cholesterol <1.16 mmol/L in men
  - o and <55 mg/dl in women
  - o Triglycerides >2.3 mmol/L
- Age > 30y

The HOT study, which looked at aspirin prophylaxis as well, showed that aspirin significantly reduced major cardiovascular events by 36% and all MI by 30%.Other antiplatelet agents, such as clopidogrel and ticlopidine, are alternatives for those with aspirin allergy. In October 1989, the National Eye Institute of America issued guidance to opthalmologists that aspirin treatment does not appear to alter the progression of diabetic retinopathy (mild to severe nonproliferative or early proliferative diabetic retinopathy) or increase the risk of vitreous haemorrhage.[71]

The glycoprotein IIb/IIIa inhibitors improve outcomes for high-risk patients with unstable angina and non-ST-segment elevation, especially those undergoing percutaneous coronary intervention. In 2 large-scale clinical trials, the IIb/IIIa antagonists were shown to benefit both patients with and those without diabetes. They may also favorably affect rates of restenosis after percutaneous coronary intervention.[72,73] Intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin should be provided as clinically indicated, regardless of diabetic status.

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Original Article

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ACUTE MESENTERIC VENOUS THROMBOSIS: MANAGEMENT CONTROVERSIES.

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ABSTRACT

A retrospectively review of the clinical records of 57 patients of acute mesenteric vein thrombosis(MVT) treated at Riyadh Medical Complex, in five calendars 1999-2003, was performed with the view to sort the fact from controversies regarding diagnosis, non-operative management and role of second look laparotomy. The result revealed that high index of suspicion is required for diagnosis of MVT when a patient complains of diffuse abdominal pain that is out of proportion to physical signs especially in high risk persons. Contrast enhanced CT scan carries a highest, 94.4% diagnostic accuracy among all radiological investigations and should be the modality of choice for the diagnosis of MVT. The non-operative management is feasible provided the diagnosis is established before the clinical and radiological signs of bowel infarction that necessitate surgical resection of infracted bowel. The present study did not uphold the mandatory second look laparotomy which was positive in 23.5% of cases. However, the selective second look laparotomy governed by the post-operative course of the patient is more appropriate, as was positive in 50% of selected cases but without any added morbidity and mortality. Only the early diagnosis and prompt anticoagulation with judicial surgical intervention can avert the high mortality.

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INTRODUCTION

Mesenteric venous thrombosis (MVT) is a rare abdominal calamity but carries devastating consequences as a result of delayed diagnosis. Although, the disease is known since1895, Elliot[1] documented intestinal gangrene to mesenteric venous occlusion but it was only after the detailed publication by Warren and Eberhardt[2] in 1935 that the mesenteric venous thrombosis became a distinct clinical entity. Ever since many studies have discussed the probable etiologies, the clinical presentation, diagnosis and various therapeutic options have been explored. Regardless of this early recognition of pathology, the diagnosis of mesenteric venous thrombosis has remained mysterious and often only recognized at laparotomy.[3-7] Advances in new diagnostic modalities especially computerized tomography (CT) have enabled early detection of the disease.[5-6] Early diagnosis of mesenteric venous thrombosis has opened new avenues in management, as thrombus propagation leads to intestinal infarction and this process can be averted by appropriate anticoagulation, this has opened the door for non-operative management. Unfortunately there is no consensus about the initial management of MVT; some surgeons have proposed an aggressive surgical approach while others favor an initial conservative management with anticoagulation and close monitoring. Similarly, issue of second look laparotomy, mandatory or selective is yet not resolved. The present study was prompted to analyze our experience in an effort to resolve these controversies and to determine the best management strategy for this uncommon disease.

MATERIALS AND METHODS:

We retrospectively reviewed the clinical records of 57 patients of acute mesenteric vein thrombosis treated at Riyadh Medical Complex, in five calendars (1999-2003). The patient's data like presenting symptoms, past medical

Key words: Mesenteric venous thrombosis, Second look laparotomy, Intestinal ischemia

history, recent investigations, in-hospital course and final outcome were recorded carefully. The diagnosis of acute MVT was based on either positive CT scan or when discovered at laparotomy for acute abdomen. All CT scans were performed with oral and intravenous contrast, the study was considered positive for MVT when a thrombus in dilated vein or abnormal thickening of ischemic bowel wall (target phenomena) with streaky mesentery and free fluid were seen. The presence of intramural gas in bowel wall, non-enhancement of bowel wall with IV contrast or gas in mesenteric or portal vein were the signs of established gangrene of bowel. Laparotomy permitted the diagnosis of acute MVT by the presence of macroscopic changes in bowel and vessels which was finally confirmed by histopathology.

The patients with confirmed diagnosis of acute MVT on CT scan but having no signs of peritonitis like guarding and rigidity or established CT signs of gangrene were treated conservatively while surgical management was selected for other cases. In addition to usual care such as fluid and electrolyte balance, correction of anemia and antibiotic coverage, intravenous heparin was started (IV bolus of 5000 IU followed by 1000 IU/hour with infusion pump) and monitored by activated partial thromboplastin time (APTT), the dose was than adjusted to maintain APTT levels at 2-2.5 times the normal. When surgical management was selected, heparin was started immediately at the end of a laparotomy, with same dose and monitoring as in conservative management. The initial phase (5-7days) of system anticoagulation was followed by oral anticoagulation (warfrain) for 6months in the absence of any coagulation abnormality. The presence of coagulation abnormalities was investigated at 3 months, when detected the therapy was maintained for life.

The second look laparotomy was performed, mandatory or selective, as planned by surgeon at the time of operation or later on decided on basis of clinical evidences (persistent leukocytosis, fever, abdominal mass) requiring laparotomy respectively. The mortality and all complication within 30 days of operation were recorded. Sepsis was defined as any septic event leading to multiorgan failure (MOF) or death. The anastomotic leak was characterized by established intestinal fistula or leak of contrast from intestine during post-operative contrast study in selected cases. Wound infection was defined by discharge of pus from wound which was positive for bacteria's either on Gram's staining or culture & sensitivity. The duration of hospital stay was calculated for both the initial length of hospital stay and any subsequent admission related to MVT. (such as stoma closure).

All statistical analyses was carried out employing Fisher's exact test for all except for hospital stay, where student t-test was used because Fisher's exact test was not applicable, using IBM-compatible PC utilizing SPSS 10.0 for Windows (SPSS Inc., Chicago).

RESULTS:

A total of 57 cases of MVT were treated in 5 calendar years. There were 44 males and 13 females; with male to female ratio of 3.4:1 and their mean age was 47± 4.2 years. Majority, 45(78.9%) patients were found to have an underlying pathology which is liable to predispose them to acute MVT. Liver cirrhosis was the commonest (45.6%) among these predisposing factors; the others are shown in table 1, while only 12(21.1%) did not reveal to have any underlying pathology.

Table 1
Predisposing Conditions

Sr. #		Condition	Number (%)
1.		Liver cirrhosis	26 (45.6%)
	(i)	Bilharzial cirrhosis	12(21.1%)
	(ii)	Non-Bilharzial cirrhosis	14(24.6%)
2.		Ischemic heart disease	6(10.5%)
3.		Diabetes Mellitus	5(8.8%)
4.		Hypercholestrimia	3(5.3%)
5.		Renal failure	2(3.5%)
6.		Old CVA	1(1.7%)
7.		Previous DVT/MVT	2(3.5%)
8.		No predisposing factor	12(21.1%)

The commonest presenting symptom was pain abdomen which was seen in all the cases, pain usually started as vague abdominal discomfort and than progressed to moderate to severe pain. The average duration of pain was 6.8 days which ranged from 1-30days. Only 11(19.3%) cases were admitted within 48 hours of onset of symptoms. Nearly 15% of patients visited the private clinic or emergency department of hospital once or twice before finally diagnosed and admitted. Other symptoms were vomiting in 26(45.6%) with haematemesis in 10(17.5%), blood per rectum in 13(22.8%), constipation in 11(19.3%) and diarrhea in 9(15.8%) cases. The abdominal examination revealed mild to moderate tenderness in 45(78.9%) cases but clear signs of peritonitis was observed in 8(13%) cases only. The abdominal distension was observed in 12(21.1%) and 21(36.8%) patients were febrile (38°C or above) at the time of admission. The leukocytosis (WBCs >11) was observed in 41(72%) but marked leukocytosis (>16) was seen in 14(24.5%).

The CT scan of abdomen with oral and IV contrast was performed in 36 cases and proved to be diagnostic in 34(94.4%) cases. In two cases, CT was reported as normal, one patients developed sign's of peritonitis within 24 hours of observation and at laparotomy found to have MVT, while in other case the diagnostic laparoscopy was performed for persistent abdominal pain which showed a small gangrenous segment with early ischemic change in jejunum, so converted to laparotomy. The ultrasonograpghy had very low diagnostic yield, was diagnostic in 7 out of 21 cases. The traditional method of four quadrant tap was used in 7 cases only and revealed blood stained aspirate in 3 cases. Only one case was operated on the basis of positive tap and ultrasonograpghy and found to have MVT, in all other case the diagnosis was based on positive CT scan. Hence,

Table 2
Mandatory Vs Selective Second Look Laparotomy

Sr.	Parameters	Mandatory n=17	Selective n=29	P-value
1.	Positive laparotomy	4(23.5%)	3(50%)	0.23916
2.	Morbidity			
	(i) anastomotic leak	1(05.8%)	1(3.4%)	0.6077
	(ii) intra-abdominal collection/abscess	2(11.7%)	3(10.3%)	0.6188
3.	Mortality	3(17.6%)	5(17.2%)	0.6343
4.	Hospital stay (mean)	21.1±3days	19.8±3days	0.1631

*P-value of less than 0.05 is significant.

preoperative diagnosis was established in total number of 36(63.2%) cases and 21(36.8) cases were diagnosed as incidental finding during laparotomy for acute abdomen.

The 11 cases without clinical evidence of peritonitis and no sign of gangrene of bowel (intramural gas in bowel wall, non-enhancement of bowel wall with IV contrast or gas in mesenteric or portal vein) on CT scan were managed with anticoagulation alone, while other 25 cases underwent laparotomy. The most consistent findings at operation were hemorrhagic ascites, congested edematous mesentery and thrombosis of venous arcades with palpable arterial pulsation and varying length of ischemic bowel segment. All macroscopically infracted bowel segments was resected, length of involved segment ranged from 25cm to almost total small bowel, caecum and ascending colon with average of 75cm. Resection and primary anastomosis was performed in all except 07 cases, 35 cases had end to end small bowel and 04 cases enterocolic anastomosis. While the remaining 07 cases temporary stoma (ileostomy) was established where as result of advance peritonitis or due to general condition of the patient, surgeon felt unsafe to perform anastomosis. The general preoperative and postoperative management was comparable in all cases.

The planned (Mandatory) second look laparotomy, as decided by the surgeon at the time of first operation was performed usually 48 hours later but only 4(23.5%) cases required further resection. In selective group, 2nd look laparotomy was decided on clinical grounds (such as persistent fever or leukocytosis or abdominal sign's) in 6/29 cases which turned out to be positive in 3(50%) of cases. The morbidity and mortality in two groups (Mandatory vs. Selective) is compared in table 2. The non-operative management was successful in all except two patients, one patient was not showing any sign of improvement, under went exploratory laparotomy on 3rd day of conservative management and found to have a small segment of ischemic bowel, hence resection and anastomosis was performed. Another patient died on 6th day of conservative management due to underlying medical disease (ischemic heart disease) without any clinical evidence of failure of conservative management. The complications encountered in operative group are shown in table 3. The anastomotic leak was managed conservatively by total parenteral feeding and other general measures in one case but other case required operative intervention (drainage of abscess and ileostomy). All intra-abdominal collections were managed by CT guided drainage and IV antibiotics. Among the non-surgical complications, the progression of thrombus into splenic vein lead to infraction of spleen and one patient developed splenic abscess required splenectomy. The overall mortality was 9(15.8%), which was evenly distributed in all three groups, all deaths except one in conservative group resulted from septicemia leading to multi-organ failure and were attributed to the MVT. The hospital stay was significantly shorter in non-operative group as compared to operative group, as shown in table 4.

Table 3
Complications

Sr. #	Complications	Number (%)
A.	**Surgical Complications**	
1.	Anastomotic leak	2(4.3%)
2.	Intra-abdominal collection/abscess	5(8.8%)
3.	Chest infection	8(14.1%)
4.	Wound infection	7(12.3%)
B.	**Non-Surgical Complications**	
1.	Upper GI bleeding	4(7.1%)
	(i) Esophageal varices	3(5.4%)
	(ii) Duodenal ulcer bleeding	1(1.7%)
2.	Splenic infarction/abscess	3(5.4%)
C.	**Overall mortality**	**9(15.8%)**

DISCUSSION:

Acute MVT is defined as a thrombus in the mesenteric vein with bowel ischemia, regardless of its severity[3]. MVT is certainly a rare but distinct clinical entity which should not be confused with other causes of mesenteric ischemia. It represents about 10-20% of all bowel infarctions and carries relatively better prognosis as compared to arterial thrombosis.[4] Despite the increasing awareness of disease and modern diagnostic gadgets, delay in diagnosis is frequent which is one of the main reason for reported higher mortality rate of 15-40% in the literature.[4-7] The main reason for delay in diagnosis are non-specific abdominal signs and symptoms of MVT despite progressive or advanced disease.[5] In spite of the vagueness of symptoms, the hallmark of MVT remains to be a diffuse crampy abdominal pain that is out of proportion to physical findings. Classically, the pain is of several days to even week's duration, this has been observed by many authors[4,6] as well as the average duration of 6.8 days pain in present study support this view. Furthermore, such pain is usually associated with negative workup for common causes of abdominal pain.[7] Another interesting point noticed in the present study was that almost 15% of patient seek medical advice one or two times before finally diagnosed as MVT. This highlights the fact, not to ignore the symptoms in absence of physical sign's and negative laboratory tests. High index of suspicion and liberal use of CT scan in such cases is the key for the early diagnosis of MVT.[5, 7-8]

Table 4
Operative Vs Non-operative

Sr.	Parameters	Operative n=46	Non-operative n=11	P-value
1.	Mortality	8(17.4%)	1(9.7%)	0.4415
2.	Hospital stay (mean)	20.5±3days	13.1±3days	<0.0001

*P-value of less than 0.05 is significant.

The MVT may be primary or idiopathic or may be secondary to a known co-morbid disease. The incidence of primary is continuously decreasing as a result of the increasing information of predisposing conditions.[7-9] The common disorders associated with MVT are, Liver cirrhosis, previous history of DVT, malignancy, pancreatitis, chronic real failure and hypercoagulable states, such as deficiencies of antithrombin III, protein C and protein S[4,10]. In the present study, 79% of cases were secondary to such predisposing disorder which is consistent with 81% of Abdu et al[11] and many others.[1,5,7,10] Among the predisposing conditions liver cirrhosis was the commonest and many of these patient are known to portal hypertension and esophageal varices. Hematemesis and melaena, although rare but have been a presenting feature in advance cases of MVT; also in present series 10 & 13% cases presented with haematemesis and melaena respectively, hence unnecessary endoscopies in such cases may lead to delay in diagnosis.[9] However, overall the presence of such co-morbid conditions in a case of vague abdominal pain should alert an intelligent physician about the possibility of MVT and investigation on this line should help in early diagnosis of MVT.[7,9]

The physical findings and laboratory data is neither sensitive nor specific for the diagnosis of MVT; hence, they are not of great help in establishing a diagnosis.[5] Leukocytosis was observed in 72% of cases, out of this only 24.5% had WBCs count of > 16000 and all of these cases with severe leukocytosis found to have bowel gangrene but, this can be seen in many abdominal catastrophes.[9] Abdominal radiographs often demonstrate nonspecific ileus with dilated, fluid-filled bowel loops and do not play any part in diagnosis.[11] Duplex ultrasonograpghy has been reported to have an 80% overall sensitivity in the Mayo clinic study in demonstrating thrombus or absence of flow in the MV.[12] But, in present study the results of duplex scanning was not very promising, only positive in 33.3% of cases.[9,13] Ultrasonography, in additions to being operator dependent does not provide any information on the secondary effects of MVT which are very important in current management, therefore of very limited value in diagnosis of MVT.[13,14] CT scan with oral and IV contrast is highly sensitive, accuracy ranging from 90-100%, demonstrate direct & indirect signs of MVT which helps in management that's why, has become investigation of choice for diagnosis of MVT.[5,9,13-17] Other methods like MRI, angiography and laparoscopy are also useful in diagnosis of MVT. MRI offers no distinct advantage over CT scan in diagnosis, except avoidance of radiation exposure and can be used in patients with contrast hypersensitivity or renal impairment.[5] Angiography has comparable diagnostic value as CT but being more invasive and without any additional benefit is not the first line investigation and neither was used in present study.[4,9,13] Diagnostic laparoscopy is an other upcoming tool for diagnosis of bowel ischemia but as requires general anesthesia, the real benefit of pre-operative diagnosis is lost. Unfortunately, because of non-availability in emergency OR, our experience is limited to one cases in which it was used after negative CT, where it turned to be diagnostic. However, it needs further evaluation to decide the fate of laparoscopy in the diagnosis of MVT.[18]

The goal of treatment is to prevent or limit bowel gangrene. When bowel infarction is present as evident by sign's of peritonitis and supplemented by radiographic evidences, surgical resection of the involved bowel is mandatory.[7,9] However, there is some controversy regarding the extent of resection. Traditionally, wide resection beyond the site of involved margins has been advised because thrombosis may extend further than the visibly infracted bowel.[5] The attempts at revascularization of larger veins with thrombolytic agents or mechanical thrombectomy has not met with significant success and presently neither recommended nor we used in our study.[4,14] Recently, the early postoperative or even intra-operative full heparinization has demonstrated to decrease both the risk of propagation and rethrommbosis and eventually improves survival.[6 11,19,20] This has lead to limited resection of grossly infracted bowel. Nevertheless, if one is suspicious of viability of remaining bowel, is an indication of "second look" laparotomy rather than further resection of doubtful area.[7,9,21] The mandatory second look laparotomy in itself has given rise to controversy, liberal use resulted in too many negative second look laparotomy, as was observed in present study as well as by others,[4,9,22] which consequently pose extra socioeconomic burden. This issue can be address by selective use of second look laparotomy, hence reducing the incidence of negative explorations with comparable rate of morbidity and mortality as reported in literature and also validated by present study.[9,22.]

Historically, the management of MVT is mainly surgical, as was stated by Grendell and Ockner[23] in a review on mesenteric thrombosis "successful therapy was dependent upon early surgical exploration, performed either because of presumptive diagnosis, or because some undiagnosed catastrophic intra-abdominal process was suspected." Later on, Abdu et al.1 1 showed that the use of anticoagulants as an adjunct to bowel resection significantly decreases the mortality and improves the survival of patients, this highlights the role of anticoagulation. Recently, with growing awareness of disease and sophisticated diagnostic modalities has made early and preoperative diagnosis of MVT a reality. Furthermore, realization of the fact that bowel ischemia without transmural necrosis is potentially reversible with anticoagulation,[3,11] this has opened the door for non-operative management of MVT. Finally, the conservative management of MVT will only be practicable, if we can diagnose the MVT with certainty by means of noninvasive abdominal imaging and secondly to establish the absence of transmural bowel infarction. Currently, the detection rate of more than 90% of cases is achievable by high- quality abdominal CT scans and also substantiated by the current study.[5,9,13-17] The evaluation of actual severity of bowel ischemia at admission is difficult. Mere dependence on peritoneal signs may not be always true, as observed by Chen et al as well as in present series.[24] However, the combination of clinical signs and absence of CT scan findings of gangrene of bowel can be used as parameters for non-operative management with reasonable accuracy.[3,7,9,25] But, the critical monitoring of progress of response of therapy remains the most important part of therapy, failure to improve or worsening in condition remains an urgent indication for surgical intervention. The ongoing studies like, intramural gastric pH measurement, bowel wall thickening by contrast-enhanced CT scanning may in future help the surgeon to decide more precisely when non-operative management is appropriate. The current data suggest that non-operative management is feasible in nearly 36% of the patients who have been reported in literature since 1990.[3,7,20,22] In our study the non-operative management was possible in 19.3%, which is quite low as compared to the reported incidence of around 36%[20,22,26] and even 80% in one study.[3] The main reasons for this are, lack awareness of disease leading to delay in diagnosis (15% multiple visits) and delayed presentation (6.8 days) results in a large number (36.8%) of incidental diagnoses, as established peritonitis by this time becomes a clinical indication for exploration. This highlights need for an overall improvement in diagnosis of MVT, which will ultimately improve the morbidity and mortality.

This study substantiate the view that non-operative management where indicated, can safely be performed with comparable mortality but with additional advantages of avoiding major resections and significantly shorter hospital stay, as shown in table 4.[3,19,20]. The overall in-hospital complications rate of 57.8% and hospital stay of 20.5 days is comparable with the reported figures.[3,19] Although, the last decade has seen significant decline in mortality but still the reported range of 13 - 26%, as well as our mortality rate of 15.8% is quite high.[3,7,9,20] Because of consistency of our results with earlier studies, we think that there was no favorable selection bias and moreover it shows the validity of our results.

Hence, we conclude that mesenteric venous thrombosis is rare but carries a significantly high morbidity and mortality as a result of delayed diagnosis. The key for early diagnosis is high index of suspicion, liberal use of contrast enhanced CT in cases of vague abdominal pain especially if the patient is cirrhotic or having prior thrombotic disorder. Anticoagulation remains the backbone of all therapies. Majority of patients require surgical intervention but early cases can be safely managed with anticoagulation alone which carries added advantages of no operation and shorter hospital stay. However, there is no substantial evidence that routine second look is mandatory, selective approach seem more appropriate.

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JK-PRACTITIONER

INTESTINAL PERFORATION AND PERITONITIS IN AIDS: CASE SERIES AND REVIEW OF THE LITERATURE

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ABSTRACT

Gastrointestinal involvement is common in patients of human immunodeficiency virus infection (HIV) and the acquired immunodeficiency syndrome (AIDS). Although the gastrointestinal complaints are frequent in these patients the incidence of acute abdominal conditions requiring surgical intervention is low (2-5%). We present a series of patients who had unusual presentations of common or AIDS- specific surgical conditions leading to bowel perforation and peritonitis.

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INTRODUCTION:

Gastrointestinal (GI) involvement is common in human immunodeficiency virus infection (HIV) and the acquired immunodeficiency syndrome (AIDS). Gastrointestinal symptoms are among the most frequent complaints in these patients and the diagnosis of AIDS is often established by detecting an infection or a neoplasm in the gastrointestinal tract. The most common GI symptom in AIDS is diarrhea followed by dysphagia, abdominal pain, jaundice, anorectal symptoms and GI bleeding. Etiology of abdominal pain in AIDS is diverse and difficult to evaluate. Although abdominal pain in patients with HIV infection may be caused by the broad spectrum of non-HIV-specific diseases in the general population, it is usually related to HIV infection and its sequelae[1]. In patients with AIDS, it is frequently difficult to verify abdominal catastrophes that require emergent surgical intervention in the setting of chronic GI symptoms, debilitation, altered mental status and absence of fever or leukocytosis. Additionally many nonsurgical conditions, that are managed medically, may mimic surgical emergencies in these patients[2,3]. Moreover common surgical conditions may have varied and unusual presentations in these patients resulting in delayed intervention[2,4,5,6]. The main objective in evaluating these patients is to first rule out life threatening complications like intestinal obstruction or perforation of a viscus[4,5,6]. Although gastrointestinal complaints are common patients with AIDS, the incidence of acute abdominal conditions requiring surgical intervention is fortunately low. Intestinal obstruction and perforation are uncommon and usually related to opportunistic infections and malignancies. A combined experience from several centers evaluating patients with HIV/ AIDS for abdominal complaints has revealed that only 2-5% of more than 2,000 patients required abdominal surgery [5,7,8,9]. However these patients have a tendency to deteriorate rapidly if a surgical condition is not address promptly. The signs and symptoms of intraabdominal pathology in patients with AIDS/HIV infection are often masked and/or altered by their inability to mount an adequate immune response and by presence of co-morbid illnesses[2]. Surgical intervention may be delayed because of the overall desire to be conservative and the general conviction that most of the abdominal complaints are related to opportunistic infections or malignancy [4,6]. Additionally, political, social and ethical issues may consciously or inadvertently affect medical decision-making. All these factors make the evaluation and management of these patients a clinical challenge. We present a series of patients who had unusual presentations of common or AIDS-specific surgical conditions leading to bowel perforation and peritonitis. The clinical picture of these usually acute surgical conditions was rather subacute and the peritonitis was "smoldering" associated with

Key words: Abdominal pain, perforation, peritonitis.

extensive fibrosis and adhesions. This may have lead to a delay in the diagnosis and management of these patients.

CASE PRESENTATIONS

CASE 1

A 47-year-old African American female with a eight year history of AIDS was admitted for evaluation of nausea, vomiting, abdominal distension and upper abdominal pain of 2 weeks duration. The vomiting was bilious without hematemasis. There was no history of melena or hematochezia. Her past medical history was remarkable for biopsy proven AIDS-related proximal ---what ?---- myopathy diagnosed six months prior and treated with steroids. She had suffered two attacks of acute pancreatitis in the month before admission. CT Scan of the abdomen revealed gallstones, pancreatic edema without abscess or necrosis. The pancreatitis was presumed to be HIV related and improved on conservative therapy.Additional past medical history was positive for hepatitis C, obesity, hypertension, anemia and steroid induced diabetes mellitus. There was a history of intravenous drug use in the remote past. The antiretroviral therapy had been stopped after she was diagnosed with a have myopathy. Current medications included prednisone, furosemide, diflucan, trimethoprim-sulphamethoxazole, glipizide and epogen. On clinical examination the patient was pale but not jaundiced. Vital signs revealed a normal temperature, pulse 78/minute, regular and blood pressure 156/104 mm Hg. Moderate pitting edema of both lower extremities was noted. A mild proximal muscle weakness without wasting in both upper and lower extremities was present. Clinical examination of the chest and cardiovascular system was unremarkable. The abdomen was distended with mild diffuse tenderness without rebound. Bowel sounds were present but decreased in intensity and frequency.

Laboratory studies revealed a white cell count of 4.1x 103/ mm3 with a CD4 count of 8% and absolute CD4 count of 104 cells / mm^3. The hemoglobin was 11 g/dl; hematocrit 34% and platelet count 184x 103/ mm^3. Other laboratory data were: serum sodium 132 meq/l, potassium 3.9 meq/l, chloride 99 meq/l, bicarbonate 28 meq/l, blood urea nitrogen 13 meq/l, creatinine 0.5 mg/dl, glucose 100 mg/dl, bilirubin 2.2 mg/dl, albumin 2.4 gm/dl, alkaline phosphatase 280 IU/l, ALT 122 IU/l, AST 115 IU/l and amylase 100 IU/L. A CT scan of the abdomen revealed large amount of free retroperitoneal air and a exploratory laparotomy revealed a large intraabdominal necrotic abscess extending into the retroperitoneum. Multiple hemorrhagic ulcers and perforations were noted in the ascending and transverse colon. There were extensive adhesions. The abscess was drained and the ascending and transverse colon were resected. The patient's condition deteriorated rapidly and she died on the second postoperative day. Pathological examination of the resected specimen of colon revealed marked chronic transmural inflammation of the bowel wall with multiple areas of necrosis and perforation.. The peritoneal surface showed marked inflammation, fat necrosis and fibrosis with organizing peritonitis. The final diagnosis was visceral myopathy with perforation and peritonitis. The visceral myopathy may have been linked to the skeletal myopathy.

CASE 2

A 42-year-old female with longstanding AIDS presented with sudden onset abdominal pain and vomiting. The latest CD4 count was 1- 4-cells/ mm^3. Antiretroviral therapy was, abacavir, nelfinavir and lamivudine. Her clinical condition improved initially with bowel rest, intravenous fluids and analgesics. However, on the 5th post-admission day the abdominal pain worsened and she developed fever. A CT scan of the abdomen demonstrated ------how do you know------ perforation of the bowel with an intraabdominal fluid collection. Initial therapy after a CT guided percutaneous aspiration, was parential antibiotics. Her condition continued to deteriorate prompting an exploratory laparotomy that revealed small bowel perforation with abscess formation. Additionally a diffuse enteritis and colitis was noted. The abscess was drained and the necrotic small bowel was resected. Aspirated specimens grew Staphylococcus and Enterococcus organisms. Pathological examination of the resected bowel revealed hemorrhagic enteritis, multiple areas of necrosis, ulceration with granulation tissue and fibrosis. A 2.5 cm large perforation of the small bowel was also noted. There was histological evidence of vasculitis with CMV inclusions in the endothelial cells. The pathological diagnosis was CMV enteritis with perforation of the small bowel. Her condition improved with intravenous antibiotics, Gancyclovir and she was eventually discharged home.

CASE 3

A 33-year-old African American man with known AIDS was admitted with a 2-month history of nausea, vomiting, lower abdominal pain and occasional rectal bleeding. A flexible sigmoidoscopy a few weeks prior to admission was normal. The past medical history was remarkable for unprotected sex with multiple female partners. He had received treatment for Pneumocystis carinii pneumonia and oral thrush in the past and was presently taking dapsone and trimethoprim. On clinical examination the patient appeared wasted, pale and dehydrated. The pulse was 80/ min, blood pressure 130/86 mm Hg and temperature was 37°C. Examination of the chest and cardiovascular system was clinically normal. Abdominal examination revealed a mildly distended abdomen, normal bowel sounds and mild lower abdominal tenderness. Rectal examination was normal and stools were guiac positive. Laboratory tests revealed hemoglobin of 8.4 gm/dl, a hematocrit of 25%, a white cell count of 8.4x 103/ mm^3 and a platelet count of 112x 103/ mm^3. Liver function tests, serum chemistry and coagulation profile were all normal.

On the second day of his admission the patient passed a large amount of dark red blood per rectum and the hematocrit fell to 21%. An upper gastrointestinal endoscopy revealed mild non-erosive gastritis. Colonoscopy revealed a large clot in the cecum overlying an ulcer with an actively bleeding visible vessel. The clot was washed and the ulcer treated with epinephrine injection. However, the patient continued to have recurrent bleeding requiring 4 units of packed red cells. An exploratory laparotomy revealed a large perforated cecal ulcer with surrounding adhesions. A right hemicolectomy was performed. Pathological examination of the resected specimen confirmed the presence of cecal ulcer, a diverticulum and multiple areas of focal hemorrhage. ------------ How about cmv or other negative histopathology----- The patient's postoperative course was complicated by acute renal failure and thrombocytopenia from which he recovered and was discharged home.

CASE 4

A 28-year-old Caucasian man with a six year history of AIDS was admitted with a 2-week history of nausea, vomiting, abdominal pain and fever. He had been seen in the emergency room two weeks prior to admission for the same symptoms. Basic laboratory tests and liver functions were normal at that time and a plain x-ray of the abdomen had revealed a large amount of stools in the colon. He was treated with an enema and intravenous fluids and discharged home. His past medical history was remarkable for unprotected sex with multiple female sexual partners, Pneumocystis carinii pneumonia and positive PPD. He was currently taking retrovir and bactrim. On clinical examination his pulse was 115/ min, blood pressure 132/90 mm Hg and temperature 38.8 0C. Clinical examination of the chest and cardiovascular system was normal except for the tachycardia. Abdominal examination revealed distension; right upper and lower quadrant tenderness and guarding without rebound. Bowel sounds were decreased.

Laboratory tests revealed a hemoglobin of 16 gm/dl, white cell count of 6.7x103/ mm^3 and platelet count of 142x 103 /mm^3. His CD4 count was 101. Serum chemistry, liver function tests and serum amylase were normal and blood and urine cultures were negative. Sputum staining for acid-fast bacilli and Pneumocystis carinii and serological tests for Cryptococcus, Toxoplasmosis and CMV were all negative. Chest x-ray was normal except for increased interstitial markings. An ultrasound and CT scan of the abdomen revealed a phlegmonous cecal mass suggestive of a perforated appendix with abscess formation. Diffuse echogenic foci were noted in the liver. An exploratory laparotomy revealed a large retrocecal inflammatory mass surrounding a perforated retrocecal appendix with extensive indurations and adhesions. Right hemicolectomy was performed. Pathological examination of the specimen revealed edematous thickened cecum and terminal ileum with a black leathery perforated appendix. The appendix showed evidence of transmural inflammation, congestion and hemorrhage. Extensive pericolonic abscess formation and fibrous adhesions were noted. His postoperative course was complicated by recurrent polymicrobial wound infections and wound dehiscence requiring multiple repairs. Peritoneal fluid cultures were negative for acid-fast bacilli, bacterial and fungal cultures. The patient was empirically treated with antibiotics and antitubercular therapy. The bactrim, AZT and lamivudine were continued. He developed incisional abscesses, which required surgical drainage many times eventually resulting in an enterocutaneous fistula.

CASE 5

A 35 year old Caucasian male, with a three year history of HIV disease was admitted with a 2 week history of nausea, vomiting and vague upper abdominal pain. He was seen, once in the emergency room and once in the clinic for these symptoms and treated with H$_2$ blockers. However the symptoms persisted and the pain increased in intensity. On the day of admission patient also complained of right shoulder pain and worsening of the abdominal pain with respiration. The past medical history was remarkable for history of intravenous drug use and hypothyroidism. Concurrent medications were zidovudine, zalcitabine, bactrim and synthroid. On clinical examination he appeared dehydrated and was distressed with pain. The pulse was 84/min, blood pressure 140/54 mm Hg, respiratory rate 20/ min and temperature 37.4 0C. Clinically examination of the chest and cardiovascular system was normal. Abdominal examination revealed a distended abdomen with decreased bowel sounds. There was epigastric and right upper quadrant tenderness and guarding without rebound. Laboratory data revealed hemoglobin of 15.3 gm/ dl, white cell count of 11.3x 103/ mm^3 and platelet count of 175x 103/ mm^3. The CD4 count was 117. Serum chemistry, liver function test and serum amylase were normal. A plain x-ray of the abdomen demonstrated free air in the peritoneal cavity. An exploratory laparotomy revealed purulent, cloudy and foul smelling fluid in the peritoneal cavity. A gangrenous appendix with an ileal perforation, a large periappendicular abscess and extensive adhesions were noted. Appendectomy and repair of the ileal perforation was performed. Pathological examination of the resected specimen revealed appendicitis with the whole specimen replaced by a suppurative mass. Gram stain of the peritoneal fluid demonstrated gram-negative bacilli. Culture of the fluid grew Streptococcus viridians, Bacteroides fragilis and B vulgatus, Candida lipolytica, Porphyromo species and Prevotella species. Patient was treated with broad-spectrum antibiotics and antifungal agents. The postoperative course was complicated by wound dehiscence, which required repair.

CASE 6

A 43-year-old Caucasian man with known HIV disease presented a 2-week history of intermittent nausea, vomiting, rectal pain, bleeding and constipation. He had been seen with the same symptoms 4 weeks prior to admission and noted to have a ulcerated warty anorectal mass. Biopsies revealed moderately differentiated squamous cell carcinoma. A CT scan of the abdomen had revealed a large mass almost filling the rectum and extending into the perirectal fatty planes.Multiple pelvic, periaortic and inguinal nodes were present. At that time further evaluation and treatment had been refused. Past medical history was remarkable for unprotected sex with multiple female partners, hepatitis C and anemia. On clinical examination he was pale, cachectic, dehydrated and somnolent. The pulse was 90 per minute, blood pressure 116/46 mm Hg and temperature 37° C. Clinical examination of the chest and cardiovascular system was normal. Abdominal examination revealed a distended abdomen with diffuse tenderness with out rebound and normal bowel sounds. Multiple firm lymph nodes were palpable in both inguinal regions. He refused a rectal examination because of pain and tenderness.

Laboratory data revealed a Hb of 7.2-gm/ dl, a WBC count of 11x 103/ mm³ and a platelet count of 324x 103 /dl. The CD4 count was 174. Serum chemistry was normal. Liver function tests revealed an albumin of 2.3 g. dl, alkaline phosphatase 99 U/l, AST 90 U/l, ALT 74 U/L, bilirubin o.8 mg/dl and calcium 10.2 mg/dl. A plain x-ray of the abdomen demonstrated dilated loops of small and large bowel, predominantly in the area the cecum and a large amount of free intraperitoneal air. The patient and his family refused any surgical intervention and requested only comfort measures. Patient died on the third post-admission day. An autopsy revealed cloudy and opaque peritoneal surfaces with 200 CC of turbid tan fluid in the peritoneal cavity. Massively dilated friable loops of small bowel and cecum were noted adherent to each other and to the liver. The pelvis was filled with a large hard mass with adherent loops of bowel. After dissection a large grayish tumor was seen extending form the anus to the distal rectum, the perirectal soft tissue and the bladder. The cause of death was reported to be acute peritonitis presumably from perforation of the massively dilated cecum. The exact site of perforation was difficult to discern. Histology of the tumor revealed moderately differentiated nests of squamous cell carcinoma presumably arising from the anus.

DISCUSSION

Although abdominal pain is a common symptom in the AIDS/HIV population, " acute abdomen", requiring surgical intervention is unusual. Patients with HIV/AIDS may have an "acute abdomen" from any of the multitude of conditions that affect the general population. However they are prone to a specific set of disease processes that may present as acute abdominal emergencies. Emergency laparotomy is usually required for appendicitis, cholecystitis and AIDS-related conditions leading to GI bleeding, perforation and ischemia. Most of the AIDS-related acute abdominal conditions can be categorized into infectious or neoplastic.

INFECTIOUS CONDITIONS

CYTOMEGALOVIRUS (CMV)

Most of the opportunistic infections in AIDS patients are seen after the CD4 count drops below 200 cells/μ L. Cytomegalovirus (CMV) is the most common cause of opportunistic viral infections. The seroprevalence of CMV in the homosexual population is almost 100% (10,11). The primary infection is asymptomatic and viral reactivation occurs in immunocompromised patients especially when the CD4 count falls below 100[10,11]. The most common organs involved by CMV are the gastrointestinal tract and retina. Although CMV can involve virtually any organ in the GI tract, the colon is the site most frequently involved followed by small bowel, esophagus and stomach [12 13 14]. The pathogenesis of CMV related GI disease is believed to be submucosal vasculitis resulting in thrombosis, ischemia leading to ulceration, bowel wall thickening and ocassional gangrene or perforation.

CMV infection typically presents with anorexia, fever, diarrhea, abdominal pain and wasting[12]. CMV has been reported to be the most common cause of lower GI bleeding in AIDS patients and bleeding without diarrhea may be the initial manifestation of CMV colitis[15 16]. Bleeding may result from severe pan-colitis segmental colitis or isolated well-circumscribed ulcers. Perforation and obstruction are rare and usually require emergency surgery[17,18,19]. Perforation is most common in the area of involved colon between ileum and the splenic flexure[17]. Toxic megacolon from CMV colitis has been reported[19 20,21]. Vasculitis of the appendicular artery, which is an end artery, can lead to mucosal ischemia and ulceration leading to acute appendicitis, necrosis, perforation and peritonitis[19]. Endoscopic features vary from mucosal erythema and edema to hemorrhagic patchy or pancolitis. The lesions endoscopically are not distinguishable from those of inflammatory bowel disease[13 22]. Pseudo-tumor or polypoid inflammatory mass lesions may be seen and can cause bowel obstruction[23]. CMV can also cause spontaneous peritonitis in patients with AIDS[24]. Physical findings are nonspecific and reflect the features of underlying complications. Serological tests are unhelpful for diagnosis. Mucosal biopsies obtained endoscopically or otherwise, are the primary tools for making a definitive diagnosis. In patients presenting with a "acute abdomen", a CT scan is the diagnostic modality of choice because it allows for the evaluation of the entire abdominal cavity and provides invaluable information about complications like perforation, abscess formation and obstruction[10 23]. Management of the acute abdomen is determined by patient's health status, overall prognosis and wishes of the patient or the family. Operative management of an intestinal perforation usually involves segmental resection and an ileostomy or colostomy[25]. Primary anastomosis is generally avoided because these patients are prone to anastomotic complications like breakdown and recontamination of the peritoneal cavity. There is also a high likelihood of perforation of other parts of the bowel in the postoperative period.

MYCOBACTERIAL INFECTIONS

Mycobacterium avium-intracellulare (MAI) is one of the most common opportunistic infections in AIDS patients and the most common cause of " infectious" diarrhea[10 26]. Gastrointestinal symptoms associated with MAI infection may be mild or include abdominal pain, fever, diarrhea and weight loss[10]. MAI may cause nonspecific mucosal inflammation, edema, ulceration and thickening of the mucosal folds. Duodenum and small bowel are the most commonly involved sites[27]. MAI has been attributed to causing spontaneous bacterial peritonitis in patients with AIDS[28]. Extensive small bowel involvement may present with malabsorption and involvement of the distal ileum may present with a tender right lower quadrant mass mimicking acute appendicitis. Frank colitis, hematochezia and perforation are rare[10, 29]. Hepatosplenomegaly and a characteristic extensive mesenteric and retroperitoneal lymphadenopathy are common. Positive stool cultures suggest but do not establish GI involvement[29]. The diagnosis of disseminated MAI is established by positive blood or bone marrow cultures. Laparoscopy and guided biopsy of the intraabdominal nodes may be very helpful in the management of these patients[10, 31]. Mycobacterium tuberculosis infection is more common in the developing countries where HIV infected patients are at a higher risk for reactivation of tuberculosis. In the developing countries, 43% of HIV-infected patients develop Mycobacterium tuberculosis infection, whereas only 10% of such patients develop this in the United States[10,32]. Unlike other opportunistic infections in AIDS, Mycobacterium tuberculosis infection develops earlier in the course usually when the CD4 count falls below 400. The ileocecal area is involved in 90% cases and is the most commonly involved site in the gastrointestinal tract[33]. Ileal and colonic involvement may cause ulceration, strictures, polypoid masses and rarely bleeding[34,35]. Perforation of the bowel is rare. Patients typically present with abdominal pain, diarrhea, fever and a right lower quadrant mass[33]. Endoscopic examination may reveal small ulcers with normal intervening mucosa, nodules, mucosal thickening or polypoid masses. Fibrosis may result in deformity and rigidity of the ileocecal valve and retraction of cecum. Mesenteric and peripancreatic lymphadenopathy are commonly seen. Disseminated infection may involve the peritoneum, liver, spleen and pancreas and present with ascites or omental and mesenteric masses. CT scan is a useful in demonstrating the multiorgan involvement[31]. Diagnosis is established by acid-fast staining and culture of mucosal or nodal biopsy specimens.

CLOSTRIDIUM DIFFICILE (C. difficile)

Pseudomembranous colitis is usually seen after C. difficile overgrowth and enterotoxin release associated with the use of broad-spectrum antibiotic. C. difficile colitis is common in patients with AIDS because of frequent antibiotic use and it tends to present with an acute abdomen mimicking a surgical emergency[10]. Perforation of the colon is rare.

CRPTOSPORIDIUM AND MICROSPORIDIA

Crptosporidiosis is an opportunistic infection, usually seen when the CD 4 count drops below 200 in patients with AIDS. It occurs in about 10% of patients with AIDS in this country and 55% in the developing countries[10]. The small intestine, especially the jejunum, is most frequently involved. The gastric antrum may be involved causing marked antral narrowing. Crptosporidium is a common cause of AIDS cholangitis. Typical manifestations of intestinal cryptosporidiosis are severe abdominal pain, diarrhea, dehydration and wasting. Mucosal involvement may leads to villous atrophy, thickening of the mucosal folds and spasm. Pneumatosis intestinalis has been reported to be associated with intestinal cryptosporidiosis[36]. Intestinal perforation is very rare.

Microsporidia are important opportunistic pathogens in patients with AIDS. They can cause diarrhea, hepatitis, ascites, cholangitis or a disseminated infection. The major presentation is chronic diarrhea and wasting[37] although rarely perforation and peritonitis can occur[38].

FUNGAL INFECTIONS

Histoplasmosis is a common opportunistic infection in AIDS patients in endemic areas. Gastrointestinal involvement is seen in 5-10% of cases. The colon is the most frequently involved site. affected in 80% of cases[23]. Gastrointestinal Histoplasmosis commonly presents with fever, diarrhea and abdominal pain[39,40]. Less common presentations include ulcerative colitis[41,42], hematochezia[43], obstruction and acute abdomen from perforation[44,45]. Endoscopic and radiological signs may be indistinguishable from those of a neoplasm or inflammatory bowel disease[39,41]. Diagnosis is established by fungal stain and culture of the tissue obtained on biopsy.

Candida albicans is usually a self-limiting disease in patients with AIDS, affecting the oral cavity and esophagus. However, disseminated involvement of the GI tract may be more common than clinically recognized[39]. In an autopsy study of 109 cases, 41% had gastric involvement, 20% small bowel and 2% had colonic involvement. Necrotizing candidal enterocolitis has been reported with extensive Pneumatosis intestinalis[46]. Bowel perforation has been reported with Pneumocystis carinii colitis but is rare[47]

NEOPLASTIC DISEASE

Chronic immune immunological stimulation and impaired tumor surveillance predisposes patients with AIDS to neoplastic cell transformation. AIDS patients are more susceptible to infection by oncogenic viruses like Epstein-Barr virus and herpes virus associated with Burkitt's lymphoma and Kaposi's sarcoma. AIDS-related malignancies of the gastrointestinal tract may present with an acute abdomen, usually from complication like obstruction and perforation[10].

KAPOSI'S SARCOMA

Kaposi's sarcoma is an aggressive multifocal disease in AIDS and gastrointestinal involvement is frequent occurring in 50% of patients. It is the most common colonic neoplasm in patients with AIDS[48]. Although Kaposi's sarcoma can affect any part of the gastrointestinal tract, duodenum is the most commonly involved site. Gastrointestinal Kaposi's sarcoma typically causes multiple submucosal masses with or without ulcerations, the so-called "target" or "bulls eye" lesions[10,49,50]. Rectal involvement can be severe causing circumferential narrowing and rigidity. Kaposi's sarcoma can be asymptomatic or present with chronic diarrhea, gastrointestinal bleeding and abdominal pain[51,52]. Other reported manifestations include obstruction, perforation and toxic megacolon but they are rare[53,54]. The clinical and radiographic features of colitis associated with Kaposi's sarcoma may closely resemble chronic inflammatory bowel disease[54]. Typical endoscopic appearances are violaceous or bright red submucosal macules or nodules[49]. However endoscopic biopsies are often negative due to the submucosal location of the lesions. CT scan often reveals focal nodules or large masses with thickening of the bowel wall. Bulky lymphadenopathy may be seen and biopsy may be required to rule out lymphoma and MAI infection[49].

LYMPHOMA

Non-Hodgkin's lymphoma of B-cell origin is the second most AIDS-related neoplasm. In patients with AIDS it is typically a high grade, aggressive, diffuse, multiorgan extranodal disease[55,56]. Gastrointestinal involvement is found in about a third of patients. Terminal ileum and stomach are the most frequently involved sites although lymphoma of the colon and rectum is being increasingly reported[10,49]. Patients usually present with weight loss, pain, a palpable mass or gastrointestinal bleeding. Other reported but rare manifestations are obstruction, intussusception, perforation and ascites[57-60]. CT scan is very helpful in diagnosis, staging and planning therapy and typically shows circumferential bowel wall thickening and bulky lymphadenopathy. Surgery is usually required for palliation of obstruction, pain and bleeding although complete remission has been reported in more than 70% of patients undergoing primary resection[61].

MISCELLANEOUS

ANORECTAL CARCINOMA

Anorectal carcinoma is an unusual cancer in immunocompetent patients, accounting for only 1-2 % of cases. It is more common in homosexual men and the incidence increases dramatically with HIV infection[62]. Most of these neoplasms are associated with human Papilloma virus type 16 and 18 infection acquired through sexual contact[62]. Common symptoms associated with anorectal carcinoma are pain, pruritus and bleeding although 25% of patients are asymptomatic. A third of patients have evidence of metastatic disease at presentation. Most of these tumors are squamous cell and until recently had a poor prognosis. Small non-infiltrating tumors can be locally resected but large tumors require abdominoperineal resection. The advent of preoperative super voltage radiotherapy alone or in combination chemotherapy has greatly improved the prognosis of this disease[63].

APPENDICITIS

Acute appendicitis affects 0.1- 0.2% of the general population and may be higher in the in AIDS patients[10,64]. A study of 36 AIDS patients undergoing emergency laparotomy reported acute appendicitis in six (16.7%) patients[7] and another study of 1725 hospitalized AIDS patients revealed appendicitis in nine (0.5%) patients[65]. HIV infected patients with acute appendicitis may not develop fever or fever may already be present due to opportunistic infection in other organs. The leukocyte count may be already decreased due to the HIV infection or drugs and leukocytosis may not occur even in generalized bacterial peritonitis. Knowledge of the leukocyte count before the development of appendicitis may be helpful. The rate of perforation from acute appendicitis may be as high as 40% in AIDS patients[5]. Therefore, a prompt laparotomy or laparoscopy is required[64]. In patients with AIDS, acute appendicitis may be caused by, CMV, Mycobacterium Avium-intracellulare (MAI) and neoplastic obstruction of the appendicular base by Kaposi's sarcoma.

TYPHILITIS

Typhilitis or necrotizing colitis is a transmural inflammation of the cecum usually seen in patients with cancer and most likely associated with chemotherapy-induced neutropenia. In HIV-infected patients it is associated with CMV infection, ischemia and lymphoma and carries a high risk of perforation. Neutropenia is not invariably present[10,66]. Treatment includes supportive care, antibiotics and surgical resection of the cecum.

PNEUMATOSIS INTESTINALIS

Pneumatosis intestinalis occurs in patients with advanced AIDS and typically involves the cecum and the right colon. It has been reported in association with C. difficile, CMV, Crptosporidium and MAC infection[47]. The prognosis is usually benign although rarely perforation of the bowel can occur[67].

IDIOPATHIC COLONIC ULCER

Patients with advanced AIDS can develop idiopathic ulcers in the colon and anorectum, similar in appearance to the idiopathic ulcers in esophagus. The etiology of these ulcers is unknown. Patients may present with fever, weight loss, abdominal pain, gastrointestinal bleeding and rarely perforation[10].

The diagnosis and management of the acute abdomen remains a challenge in patients with AIDS and HIV infection. However, the dismal morbidity and mortality rates of 20% to 70% in early surgical series[7,59,68,69], have improved with better understanding of the underlying pathology and indications for surgery. More recent series have reported morbidity and mortality rates of 7% to 24%[5,60,70,71]. The hospital mortality in patients with AIDS is mainly attributed to the underlying opportunistic infections and neoplasms[8,71]. Emergency abdominal surgery for AIDS-related conditions carries a three to four fold mortality risk than other etiologies[5]. Many authors have suggested a more aggressive surgical approach to hopefully lower the morbidity and mortality associated with acute abdominal conditions in patients with AIDS[5,68,70,71]. However, there may be a loatheness on the part of some physicians to adopt an aggressive approach because of the high operative mortality and poor surgical outcome in most of these patients. These and other social and ethical factors may delay early diagnosis and timely intervention. These patients are prone to some unique pathological processes, which may have bizarre clinical presentations[72,73]. The presentations may be altered by the impaired immunity and co-morbid illnesses[2]. In all the patients presented in this series the clinical presentation of visceral perforation was rather subacute. One patient had two episodes of pancreatitis before presenting with intestinal perforation and it was difficult to ascertain the cause for perforation. Another patient had a bleeding cecal ulcer on endoscopy and also a diverticulum of the cecum, a rare entity in the western population[74]. It was difficult to ascertain if the peritonitis was from the perforated diverticuli or perforated "idiopathic ulcer", another clinical curiosity in this population of patients[16]. Patients present with nonspecific symptoms and the diagnosis of the acute abdomen is delayed because of the subacute presentation and perhaps a less aggressive diagnostic approach on the initial presentations. The pathological findings also suggested a "smoldering" type of peritonitis and extensive fibrosis associated with these perforations. Thus the clinical presentation of acute abdomen in these patients may not be truly acute because of the very nature of this syndrome. The delay in diagnosis and intervention may be due to this subacute and non-specific presentation, in addition to the other factors described above. A high index of suspicion for the subacute presentations of acute abdominal catastrophes in patients with AIDS and a more aggressive diagnostic approach would allow a timely surgical intervention and possibly improve the outcome and prognosis in these patients.

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THIN LAYER CHROMATOGRAPHY (TLC) IN DETECTION OF CURRENT NATURE OF DRUG ABUSE IN KASHMIR.

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ABSTRACT

Use of thin layer chromatography as a broad-spectrum screen for detection of drugs of abuse, as a part of this recent,larg-scale,well-designed drug abuse epidemiological study supported by the department of Science and Technology has been extremely helpful in quick diagnosis and rapid detoxification of those 61.91%of suspected substance abusers who had denied history of any drug use or abuse at first contact with the investigating team.

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INTRODUCTION

Psychoactive substance use and abuse is globally perceived as one of the alarming public health problems. No effective treatment and prevention related policy issues can be arrived at without adequate information regarding the nature and distribution of drug abuse in population and their causative factors .Widespread data in drug abuse is lacking and it is difficult to make generalizations because of regional variations[1].

The geographical location of Jammu and Kashmir makes transit of drugs possible across the state. Present prevailing disturbed conditions have worsened drug abuse scenario besides phenomenal increase in other psychiatric disorders in Kashmir[2,3]. Opiate preparations including heroine abuse has become the most serious problem in Kashmir over the past few years. Last year cases using cocaine which would cost the addict about 2000-2500 rupees per day were also detected[5]. Media reports about large scale cultivation of cannabis(charas) in southern Kashmir and seizes of large quantities of opioids mostly heroin in northern border areas like Handwara are alarmingly increasing[6,7]. Unauthorised large scale brewing and sale outlets of alcohol are becoming a common sight in the city of Srinagar and adjoining areas [8,9]. All these indicators characterizing the situation clearly reflect it as deteriorating fast .In comparison to 9.5% use of opioid based preparations during 1980 it had increased to 73.1%during 2002[6] and is worst now.

Despite such high incidence of substance abuse it is often misdiagnosed as drug abusers frequently deny or minimize their problems .The laboratory facilities help in making correct diagnosis by identifying a compound directly responsible for development of symptoms, thus immensely helping in proper treatment. Testing for presence or absence of drugs of abuse in body fluids also helps to monitor improvement of patients in treatment. Thin layer chromatography (TLC) has been used as a broad spectrum screen for detection of drug abuse. TLC results are only qualitative and cannot be quantified.[12]

The aim of this study therefore was to assess the results of use of modern scientific procedures for the first time in Kashmir for identifying different drugs and drug combinations in biological specimens of drug addicts identified through a meticulously planned community research endeavor.

MATERIAL AND METHODS:

The detection of narcotic and psychotropic substances in body fluids

Key words: Drug abuse, nature, detoxification, chromatography.

of substance abusers was carried out at the thin layer chromatography laboratory established at the hospital for psychiatric diseases Srinagar by the first author (MAM)as the principal investigator of the research project titled" community survey on substance related disorders(drug abuse) in Kashmir" assisted by the department of science and technology. More than 200 biological specimens have been analyzed by means of TLC so far during the year 2003-2004.

Methodology of TLC as a screen for detection of drugs of abuse is most inexpensive and does not require any sophisticated instrumentation. TLC results are qualitative and can not be quantified: therefore it gives positive or negative results. The major drawback of TLC is it's low sensitivity and low specificity. thus negative results of TLC are not always negative by other methods. TLC relies on a reproducible migration pattern by drug of a thin layer adsorbent (eg: silica gel coated glass plates).Characterization of a particular drug is achieved by color reaction produced by spraying the plate with coloring reagents. To accomplish this, the patient's sample is spotted along with known drugs on a TLC plate, which is put in a solvent chamber. The solvent runs up the plate, it is dried and sprayed with various reagents. The color spots of various known drugs are then compared with sample from unknown patients. The spot location is located by an R f (retention factor) number which is the ratio of distance traveled by the solvent from the original, where the sample was spotted.

The spots on TLC plate can be visualized by ultraviolet or florescent light also. In our study we have been using the ultraviolet method for detection of the spots.

Retention factor (Rf) = distance traveled by the drug/ distance traveled by the solvent

The Rf provides corroborative evidence as to identify the compound.

Table 1
Socio-demographic variables

Age	No.	%	Sec	No.	%	R/U	No.	%	Smo/N-smo	No.	%
16-25	60	35.71	Males	164	97.62	Urban	124	71.43	Smokers	156	92.85
26-35	84	50.0	Females	4	2.38	Rural	48	28.57	Non-smokers	12	7.15
36-45	20	11.91									
46-55	4	2.38									

Marital status	No.	%	Social status	No.	%	Occupation	No.	%
Unmarried	80	47.62	Upperclass	4	2.38	Students	24	14.29
Unmarried	84	50.0	Uppermiddleclass	20	11.90	Employed	72	42.56
Divorced	4	2.38	Lower middle class	124	73.82	Unemployed	28	16.66
			Lower class	20	11.90	Labourers	8	4.76
						businessman	36	21.43

Family status	No.	%	Education	No.	%	Onset age of drug use	No.	%
Nuclear	60	35.72	Graduates	12	7.15	11-15	16	9.52
Joint	104	61.90	Under graduates	64	38.09	16-20	52	30.99
Single	4	2.38	Upto matric	28	16.66	21-25	40	23.89
			Below matric	28	16.66	26-30	36	21.42
			Illiterates	36	21.43	31-35	16	9.52
						36-40	4	2.38
						40-45	4	2.38

Table 2
Nature of substance abused

Type of drug abused	Number	Percentage
Opoids other than heroin	44	26.91
Opoids+bzp	32	19.05
Opoids+cannabis	12	7.15
bzd	4	2.38
opoids+bzp+cannabis	8	4.75
opoids+alcohol+cannabis	4	2.38
cannabis+alcohol	8	4.75
cannabis+heroin+alcohol	8	4.75
cannabis+alcohol+codeine	4	2.38
alcohol	12	7.15
alcohol+opoids	4	2.38
heroine	12	7:15
alcohol+heroine	8	4.73
alcohol+heroine+analgesic	4	2.38
alcohl+codeine+cannabis	1	2.38

RESULTS AND DISCUSSION

Drugs that were found in drug abusers biological fluids are shown in the table 1.The most commonly used individual drug at present in Kashmir, by those drug abusers who usually deny use of any psychoactive substance at first contact, include opioids, cannabinoids, benzodiazepines and alcohol. The findings of this study are quite alarming. As already reported few months back in the study of patient sample of 2002, the profile of substance abusers has changed with fast increasing percentage of harder substance abusers, mostly opioid[6].

But what is more disturbing as revealed by the present study is that within a short span of two years not only has multiple drug use doubled but alcohol use which was almost nonexistent earlier has shot up to about 30% . Our earlier studies carried out to asses the out come of treatment provided to the recovering drug addicts at the non-governmental de-addiction centers with regard to the parameters like drug free status, employment status, adequacy of social functioning, the state of health in illegal activities, showed that the over all treatment results and the prognosis of drug abusers treated at NGO's de-addiction centers which are exclusively meant for drug abusers with better staff client ratio and much better chances of mutual understanding and joint effort s towards the common goal of total drug free status as compared to the drug abusers who enter a general psychiatric disease hospital based treatment program[13, 14]. However the present research and developmental activity through this project has proved a major mile stone in the direction of developing and modernizing detoxification and rehabilitative facilities in such hospital . As pointed out in an earlier study, joint efforts by all concerned government agencies, NGO's at community and individual level need to be mobilized at the earliest at least to contain this menace. Preventive measures including efforts to minimize delay and prevent people from being drug users would be helpful. Due to different conceptual models of treatment of people, involved in treating drug dependents , a well-planed strategy and co-coordinated efforts is required. Treatment in OPD, community clinic and general medical setting is cost effective and possible as well.

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SEROPREVALENCE OF CYTOMEGALOVIRUS (CMV) IN KASHMIR VALLEY - A PRELIMINARY STUDY

Rubina lone, MD; Bashir A. Fomda, MD; Manzoor Thokar, MD; Tehmeena Wani, MD; Dalip Kakru, MD; Rubina Shaheen, MD; Asifa Nazir, MBBS

ABSTRACT

Cytomegalovirus (CMV) infection in pregnant women can be responsible for fetal loss or congenital malformations. In the present study CMV specific IgM antibody was detected by ELISA in pregnant women and its association with obstetric complications was assessed. CMV specific IgM antibody was detected in 15.98% of the 1918 pregnant women studied. It was reactive in 13.93% of the 1026 asymptomatic healthy pregnant women while 18.27% of the 892 women with obstetric complications were positive for CMV specific IgM antibody. These comprised of 16.37% with recurrent abortions, 16.83% with inevitable abortion, 28.85% with intrauterine death, 10% with premature delivery and 7.14% with intrauterine growth retardation, suggesting the need for screening of women of child bearing age for CMV infection.

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Congenital intrauterine infections have been associated with congenital abnormalities, intrauterine growth retardation and intrauterine death of the fetus, as well as late sequelae such as developmental delay, blindness and deafness of the infected child[1]. Cytomegalovirus (CMV) infection during pregnancy is far more complex than other infections, due to the ability of the virus to be frequently reactivated during the child bearing age and be transmitted to the fetus inspite of maternal immunity[2].

In India, serological surveys have shown the prevalence of CMV antibodies in adult population to be about 80-90%[3,4]. However, the data regarding the occurrence of CMV infection in pregnant population is sparse. The aim of our study was; to determine the seroprevalence of CMV in our local antenatal population; to see the effect, if any, of age and parity on its seroprevalence and to find the association of CMV infection with individual risk factors during pregnancy.

MATERIAL AND METHODS

During the period between April 1998 to June 2000, 1918 antenatal women seen in the Gynae and Obstetric department of Sher-i-Kashmir Institute of Medical Sciences (SKIMS), were subjected to detection of CMV specific IgM antibody by ELISA test. These included 1026 asymptomatic pregnant women and 892 women with obstetric complications like inevitable abortion, recurrent abortions (BOH), intrauterine death (IUD), intrauterine growth retardation (IUGR) and premature deliveries.

5 ml of serum sample was collected from all the patients and send to the virology division of Microbiology at SKIMS for CMV IgM serology by enzyme linked immunosorbent assay (ELISA). The ELISA technique was performed according to the instruction of the manufacturer.

RESULTS

The mean age of the patients was 26.2 years, the mean gestation was 19.0 weeks and the mean parity was 0.95. To determine the influence of age, the patients were divided into the two age groups; these less than or equal to 25 years and those more than 25 years. However, seropositivity with regard to age was not found to be statistically significant (p = 0.571). Similarly seropositivity was analysed with respect to parity. Patients were divided into primiparous and multiparous. There was no statistically significant relationship between seropositivity and parity (p = 0.629).

Seropositivity of CMV IgM antibody seen in asymptomatic pregnant women and those with obstetric complications is shown in table 1.

Key words: CMV, ELISA, pregnancy, abortion

Table 1: ELISA positivity for CMV IgM antibody in different groups

Groups	No. of samples tests	ELISA positivity (percentage)
Recurrent abortions	507	83 (16.37)
Inevitable abortion	202	34 (16.83)
IUD	149	43 (28.85)
IUGR	14	1(7.14)
Premature delivery	20	2(10.0)
Healthy pregnant women	1026	143 (13.93)
Total	**1918**	**306 (15.95)**

CMV specific IgM antibody was positive in 163 (18.27%) of the 892 obstetric patients and 143 (13.93%) of the 1026 healthy asymptomatic pregnant women during the first trimester. Out of the 507 patients with recurrent abortions, 83 (16.3%) revealed the presence of CMV IgM antibody. CMV IgM antibody was also detected in 34 (16.83%) of the 220 patients with inevitable abortion, 43 (28.85%) of the 149 patients with IUD, 1(7.14%) of the 14 patients with IUGR and 2 (10.0%) of the 20 patients with premature delivery.

DISCUSSION

CMV is the most common congenital infection and its incidence has been estimated to be between 0.2 - 2.2% of all live births in different parts of the world[1]. In 1994, a study conducted in Malaysia involving 1688 infants with congenital abnormalities were screened for evidence of congenital CMV infection and this was detected in 11.4% of the infants, which was much higher than other intrauterine infections like congenital toxoplasmosis (1%) and congenital rubella infection (2.7%)[5].

Primary CMV infection in an individual can be detected by demonstration of CMV specific IgM antibody[6]. Also primary infection in pregnancy has a higher incidence of symptomatic congenital infections and fetal loss[7]. However, infected infants can be asymptomatic at birth with 10-15% of these subsequently developing late sequelae such as visual and auditory defects[8].

In the present study, CMV specific IgM antibody was detected in 15.98% of all pregnant women tested, indicating the substantial prevalence of infection in the local population. Out of the 1026 asymptomatic pregnant women 13.93% tested positive for the CMV specific IgM antibody revealing primary infection during the first trimester and increasing the possibility of transmission of infection in utero to the foetus.

Arti Kapil et al have reported CMV specific IgM antibody in 12.9% of pregnant women with complications[9]. In the present study, 18.27% obstetric patients showed the CMV specific IgM antibodies.

All these findings indicate that CMV infection is not uncommon in our local population. This high seroprevalence reflects the low hygienic standards and practices in our part. Also CMV can lead to substantial damage to the fetus and as the damage done in utero cannot be reverted, control of intrauterine CMV infection is important. Hence prevention of CMV infection, especially in the pregnant women is essential. Screening of pregnant women, although, cannot change the outcome of the disease but may be useful in alerting the physician for possible infection to the baby. Hence routine screening of females of child bearing age for CMV infection is desired in order to reduce the fatal outcome of the pregnancy occurring due to the CMV infection.

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PROTEUS SYNDROME

Nisar A Bhat MD, S A Kadla MD, P A Shah DM, M A Kamili MD, Ifat Hussan MD

ABSTRACT

A 20 year old female, born of non-consanguineous marriage, presented with two days history of weakness of both lower limbs and retention of urine. Clinical examination of the patient revealed multiple developmental deformities in the form of macro-Syndactyly, small and large disfiguring lipomas and other soft tissue swellings, in addition to features of non-compressive myelopathy Roentgenography revealed Macrodystrophea lipomatosa progressiva of both hands and butterfly cervical vertebrae. Aspiration cytology of soft tissue swellings confirmed the presence of lipomas and epidermal cyst. It is the first case report from Kashmir and fourth case report from india with characteristic macrodactyly.

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INTRODUCTION

Proteus Syndrome is a complex disorder comprising of malformations and over growth of multiple tissues. The disorder is highly variable and appears to affect patients in a mosaic manner. The disorder was originally described in two patients by Cohen and Hayden (1979)[1] and was designated Proteus Syndrome by Wiedemann et al (1983)[2] to denote its variability of clinical expression. It is a complex hamartomatous disorder consisting of partial gigantism of the hands and /or feet, asymmetry of the limbs, plantar hyperplasia, hemiangiomas, lipomas, lymphangiomas, varicosities, verrucous epidermal nevi, macrocephally, cranial hyperostosis, long bone over growth3 and ocular manifestations like strabismus, nystagmus, high myopia and retinal pigmentary abnormalities 4 etc. Although much has been learned about proteus syndrome in recent years, knowledge is still evolving rapidly. We present a case of proteus syndrome with some features which have not been reported so far.e.g. Butterfly cervical vertebrae, absent mammary ripple and syndacytly.

CASE REPORT

A twenty year old female born of non consanguineous marriage was admitted with two days history of sudden weakness of both lower limbs and retention of urine. As a result of this weakness the patient was unable to stand or walk. There was no history of any recent febrile illness, upper respiratory catarrh or vaccination, prior to onset of these symptoms.

The patient had large hands with fused fingers and swelling over the back since birth. As she grew up, her hands and fingers became progressively disproportionately enlarged, and the swelling over the back also increased in size. In addition to this, swellings also appeared on back on right side just below the scapular region and another in right hypochondrium.

The patient was born as full term normal delivery at home. She was 5th in birth order with all family members apparently normal. There was no significant history in her antenatal, natal and post- natal periods.

Examination of the back revealed a swelling covering whole of the right scapular and interscapular region with extension to lower part of neck giving it a webbed appearance (Fig I). The swelling was soft in consistency with well defined margins. In addition to this, another swelling of 7x 8 cm was present just below right scapular line (Fig

Key words: Macrodactyly, Macrodystrophea lipomatosa progressiva, Transverse myelitis.

II). It was soft in consistency, slippery to touch with well defined margins.

Examination of the breasts revealed normal right breast. Left breast was enlarged, and pendulous with well-developed areola but only rudimentary non-punctate nipple.

Examination of hands revealed following features (Fig III, IV & V).

A.) Right hand, hypertrophied with normal thumb. Macrodactly of index and middle finger. Syndactyly of ring and little fingers, both of which were hypertrophied. Whole of the right hand revealed ulnar deviation. The palmar skin was thick, rugose, with gyriform convolutions. The skin on dorsum revealed prominent superficial vessels. There was a swelling in the lower part of right arm just near elbow joint. The swelling was similar to other swellings and measured 4x8 cm. Whole of the right fore-arm was hypertrophied with prominent veins over the skin. No bruit was heard. Nails were normal.

B) Left hand of the patient revealed normal thumb, index and little fingers (FigIV). No macrodactly. Syndactly of middle and ring fingers, both of which were of normal size. Ulnar deviation of hand. The palmar side revealed thick, rugosities with gyriform convolutions. There were prominent superficial vessels over the skin and on dorsum of hand. The fingers of the left hand were in the attitude of flexion (110°). There was inability to suppinate the left hand. There was flexion contraction at wrist. Left fore-arm too was hypertrophied but not as large as right fore-arm. Prominent veins were also visible on left fore-arm. Nails were normal. The upper arms, lower limbs and feet were normal with respect to morphology. The examination of chest and CVS was normal. The examination of abdomen revealed an extra abdominal soft non tender swelling of 10x12 cm in right lower quadrant with striae on its overlying skin (Fig III). There was no organomegaly. The examination of CNS revealed paraplegia of upper motor neuron type with palable urinary bladder with sensory level at T 8. Examination of fundi was normal.

ANTHROPOMETRIC DATA of patient revealed (in inches)

- Height = 65 - Head circumference =21.4 - Girth of right middle finger = 12
- Arm span = 60 -Upper segment =31 - Lower segment =34
- Right fore-arm (length) = 10 - Right shoulder to elbow distance = 13
- Left fore-arm = 11 ½ - Left shoulder to elbow distance = 16
- Right hand, wrist to tip of middle finger = 13 - Palm span =8x14
- Left hand, wrist to tip of middle finger = 12 - Palm span =5x7
- Weight =76 kg

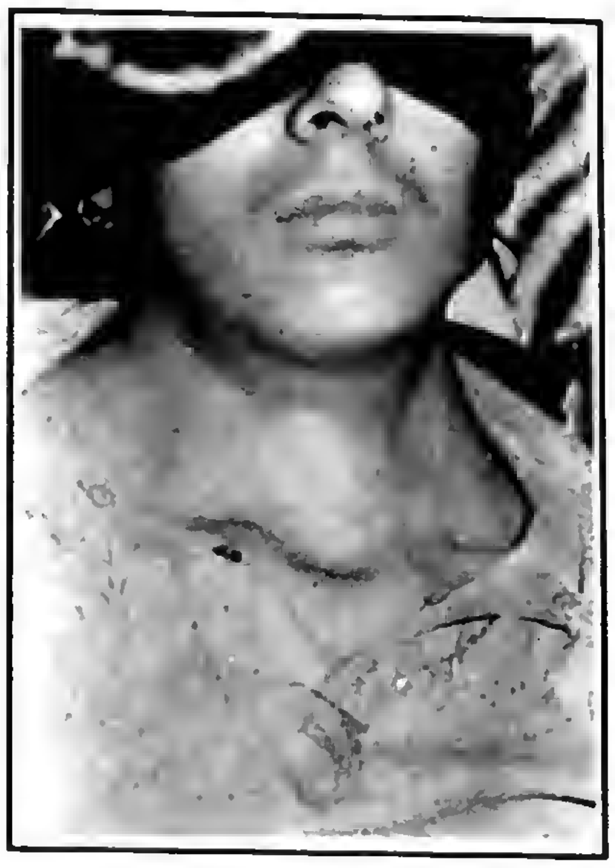

Figure I. Webbed neck

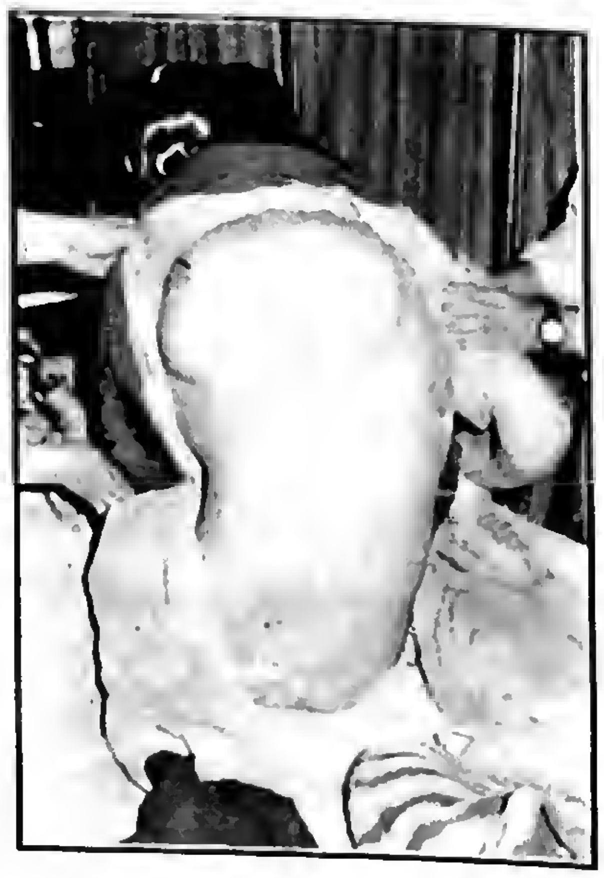

Figure II. Multiple swellings on the back

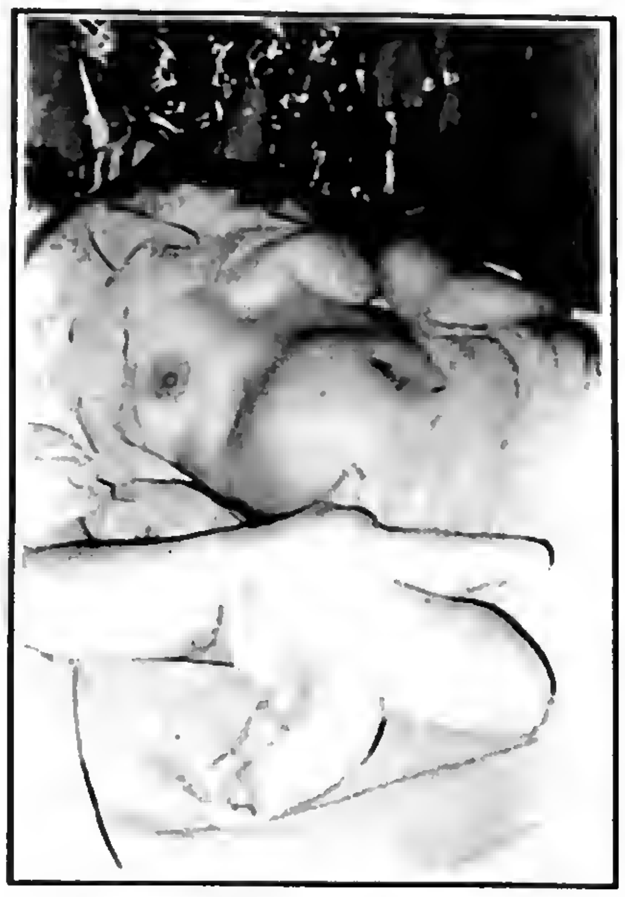

Figure III. Pendulous large left breast with nonpunctate nipple and righthand

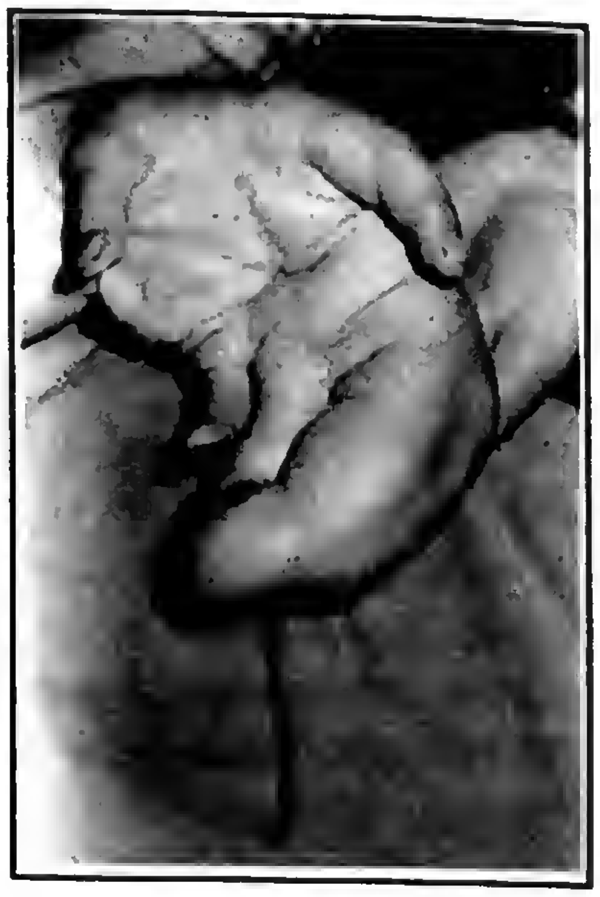

Figure IV. Left hand

INVESTIGATIONS REVEALED:

1. Normal urine analysis, hemogram, KFT, CSF and LFT. ECG was also normal.
2. The radiological investigation showed butterfly cervical vertebrae (Fig VI)
3. X-ray survey of chest (P/ A view), long bones, lumbo-sacral spine and CT myelography were also normal.
4. X-ray survey of hands revealed Macrodystrophea Lipomatosa progessiva of both hands.
5. FNAC of the swellings revealed them to be lipomas with exception of the swelling below right scapular area, which revealed features of epidermal cyst.

The patient was managed as a case of transverse myelitis. She was put on indwelling catheter and physiotherapy. With aforementioned clinical and laboratory parameters, a diagnosis of proteus syndrome with no compressive dorsal myelopathy (segment level D8) was made. Her weakness improved and there was no residual weakness.

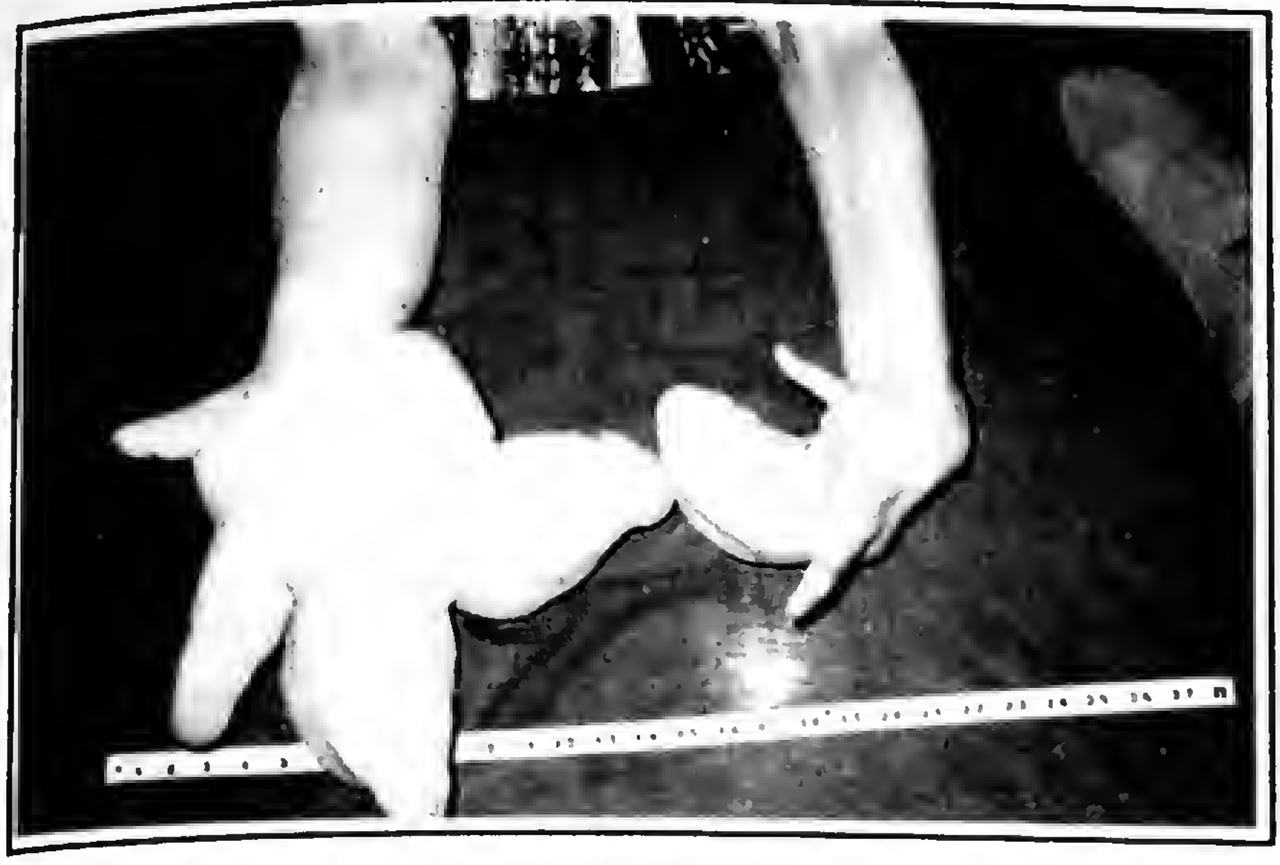

Figure V. Both hand

DISCUSSION

Proteus syndrome is a congenital disorder with varied clinical manifestations -Happle(1987)[5] hypothesized that the syndrome resulted from a somatic alteration of a gene leading to mosaic effects that would be lethal if the mutation were carried in a non mosaic fashion. This potentially explains the variability among and within patients. but has led to diagnostic confusion. The first National conference on proteus syndrome for parents was held at the national Institute of Health in Bethesda, Maryland from March[18-20], 1998 and recommendations were given on diagnostic criteria, differential diagnosis and guidelines for evaluating patients[6]. The general characteristics of mosaic distribution of lesions, progressive course and sporadic occurrence are considered mandatory, regardless of specific manifestations in a given patient. Connective tissue nevi are common and are facultative but not obligatory i.e. they may or may not be present. When present, a connective tissue nevus is almost pathognomonic for proteus syndrome and kept in specific criteria (Category A). Category B includes[1], Epidermal nevus;[2],Disproportionate overgrowth in one or more limbs (arms/legs/hands/feet/digits), skull (hyperostosis), external auditory meatus (hyperostosis), vertebrae (Megaspondylodysplasia), visceral enlargement (spleen, thymus) and [3], Specific tumours before end of second decade (either one). bilateral ovarian cystadenomas, parotid monomorphic adenoma. Category C includes : 1. Dysregulated adipose tissue (either one) - lipomas, regional absence of fat ;[2]. Vascular malformations (one or more)- Capillary malformations, venous malformation, lymphatic malformation[1]. Fascial phenotype- dolichocephaly, long face, minor down slanting of palpebral fissures and/or minor ptosis, low nasal bridge, wide or anteverted nares, open mouth at rest. Our patient fulfilled the general criteria and had features from category B and C. Our patient had butterfly cervical vertebrae, absent mammary nipple (left side) and syndactyly. Although much has been learned about proteus syndrome in recent years (Cohen 1993[3], Biesecker etal 1998[7], knowledge is evolving rapidly. The recommendations for diagnostic criteria are considered tentative because future clinical and molecular studies may necessiate modification after scanning patients of proteus syndrome in future.

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JK-PRACTITIONER

FILLING OF LARGE HUMERAL DEFECT IN A TWO YEAR OLD CHILD BY ILIZAROV TECHNIQUE

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ABSTRACT

Ilizarov technique of bone transport is now an established method of treatment of large bone defects, however, filling of such defects in children pose multiple problems to the treating surgeons. We present a case of large humeral defect due to osteomyelites in a two-year-old child treated by bone transport using a modified external fixator. A 7.5 cm defect in humerus was filled with a healing index of the regenerate of 1.02 months/cm. The total duration of fixation was 8 months. Mild pin tract infection during the fixation period was the only problem encountered.

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INTRODUCTION:

Filling of large bone defects is one of the most difficult problems in reconstructive surgery. Large defects in bone may result from trauma, infection or as a result of resection of big segments of bone for various pathologies. Small defects have traditionally been treated by bone grafting, however, it takes long consolidation time, may have rejection, sequestration and require prolonged immobilization for filling large bone defects. Isolated free fibular grafts again need long periods of immobilization and have a high rate of sequestration. Though the vascularised fibular grafts have the advantages of better resistance to infection and better incorporation, the technique needs microsurgery and is technically demanding. Ilizarov's technique of bone transport has produced remarkable results in filling of such large bone defects. The technique involves lengthening distraction of one of the bone fragments to fill the defect. Management of large defects of upper limb in very young children is very diffcult in terms of fixation of small bone fragmets which have been rendered week by disuse porosis. We present a case of large humeral defect in a two-year old child filled by bone transport over a modified external fixator to avoid the bulky rings of the Ilizarov frame.

CASE REPORT:

A two year old male child suffered an attack of a cute steomyelites of his right humerus when he was one year old. Repeated drainages and sequestrectomy left a big diaphyseal gap in the humerus. Patient was brought to our OPD for treatment of the deformity. Examination revealed a frank non-union of humerus with stiff elbow and shoulder as a result of prolonged Plaster of Paris immobilization. X-Rays showed a large diaphyseal defect with porotic bone fragments with tapering ends. Ilizarov bone transport was planned using a uniplanner fixator. The external fixator was pre-constructed to decrease operation time and consisted of three curved connection plates connected by a threaded rod. Surgery was under taken under general anesthesia. The defect site was opened and the intermediary fibrous tissues removed. The bone ends were freshened and the medulary cavities opened on either side. A small Krishner wire was passed in a retrograde manner to maintain the alignment of the bony fragments. The fixator was next mounted on the humerus using small diameter half pins, two in each of the connection plate. To add to the stability of the fixator, fixation was performed across the elbow. Through a small incision corticotomy was performed in the supracondylar region. After a latency of five days bone transport was started by turning the nuts on the threaded rod at a rate of 0.25 mm four times a day. Once the distraction was completed the fixation across elbow was removed to allow range of motion exercises of the elbow. At the time of docking the bone ends were freshened again and small cancellous bone graft

Key words: Osteomyelites, Non-union, Bone transport, Ilizarov technique

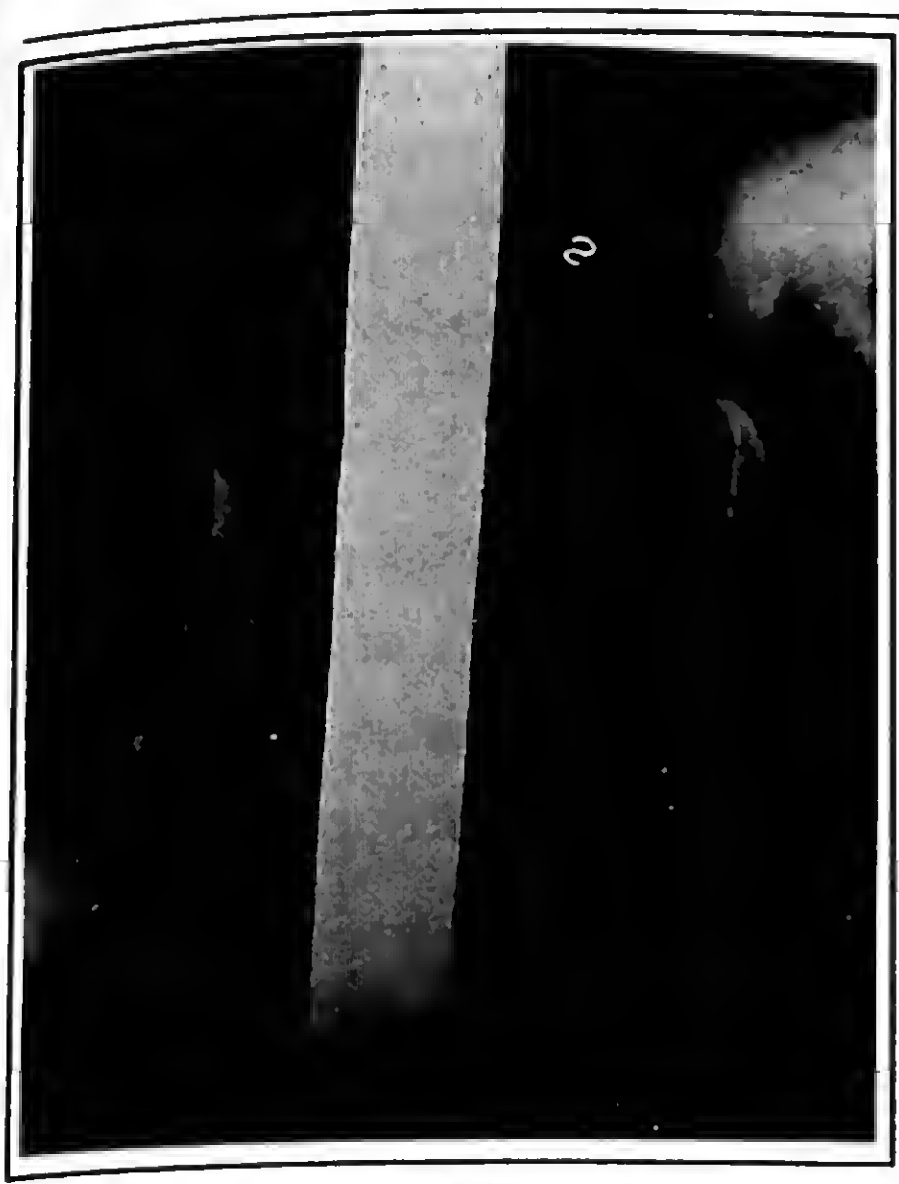

Figure 1. Pre-operative radiograph showing diaphyseal defect.

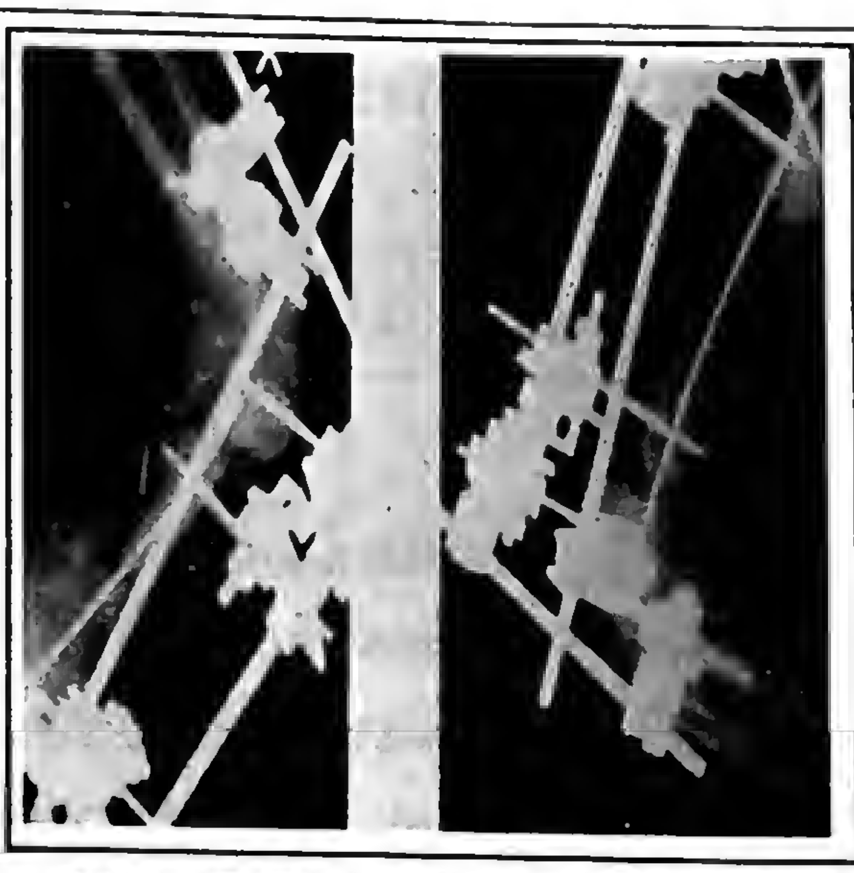

Figure 2. Post operative radiograph showing bone transport in progress

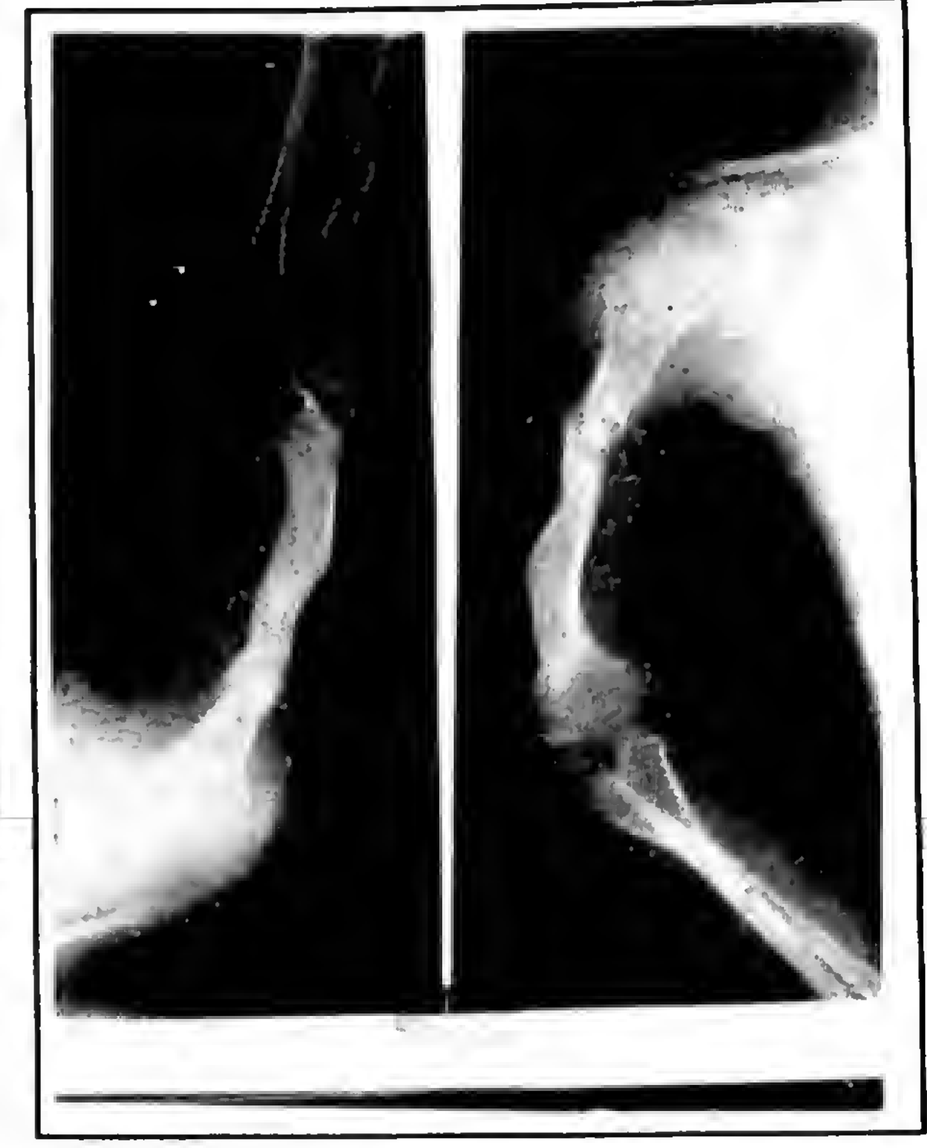

Figure 3. Radiograph showing elimination of defect by bone transport

added to facilitate union. The external fixator was left in place till the union at the docking site was confirmed radiologically. At this time the external fixator and the Krishner wire were removed and the arm protected in a humeral brace. The patient was encouraged to do physiotherapy. The total duration of external fixation was 8 months. The elbow range of motion improved to 1° to 10° arc. Two pins had mild pin tract infection during the period of fixation,which resolved by antibiotics and dressings. The parents were happy with the final result.

DISCUSSION:

Ilizarov technique is a very effective method of treating non-unions[1]. Catagni et al in his report of 16 patients of humeral non-unions achieved union in 14 patients using Ilizarov technique with few complications[2]. Many reports present similar result.[3,4,5] On the other hand Haidukewych GJ et al in a report of 15 infected non - unions of humerus treated by methods other than Ilizarov technique found difficulty in achieving union in infected non union in comparison to the aseptic non union[6]. Ilizarov technique has produced remarkable results in filling large bone defects[7,8]. Golyakhovsky V. Fankel VH, using Ilizarov bone transport were able to fill defects ranging from 4 to 16 cms[9]. Similarly Ilizrov technique has been very effective in the management of non-union where multiple surgical interventions were already done[10]. In a comparative study between Vascularized fibular grafting and Ilizarov bone transport for filling large bone defects, Song HR found better bone results with the bone transport group[11]. They advised careful monitoring of the circulation and early intervention surgery to avoid vascular failure in vascularized fibular grafting and the use of bone grafting at the docking site in the internal transport group to facilitate union. In our patient we achieved excellent result using bone transport over a modified uniplanner fixator to overcome the difficulty of fixation and to avoid the heavy frame ring fixator. Mild pin tract infection during external fixation was not a major concern. We believe that use of a uniplanner external fixator could be a valuable option for filling large bone defects in very young children.

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AN UNUSUAL FOREIGN BODY IN THE URINARY BLADDER

Syed Sajjad Nazir M.S; Baldev Singh Wazir M.S; FAIS; FICS, Shagufta Qazi MD.

ABSTRACT

Many cases of self introduction of foreign bodies into the bladder have been reported. Different items have been found (light bulbs, fruit kernels, screws, pebbles, wires etc.) and most were associated with mental illness, senility, psychiatric abnormalities or for sexual purposes. We report a case of transvesical foreign body following penetration of the rectum secondary to a fall on log of wood.

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INTRODUCTION

A 27 year old male presented with increased frequency of urine, and burning at the end of micturation. A plain X-ray of the abdomen including pelvis was normal . Ultrasonography revealed a rod shaped vesicle calculus.

The patient had suffered a rectal injury three months earlier. He had a fall from 8 feet height on a log of wood and sustained an injury in the perineal region on the right side. An examination was performed which revealed a clean incised wound, bleeding actively measuring 5cms and extending 1cms away from anus laterally on right side which was stitched. Proctoscopy revealed a hyperaemic area on the anterior wall of the rectum. Patient developed haematuria for three days which was treated conservatively by antibiotics (ciprofloxacillin).

Following the discovery of the calculi, the patient underwent cystoscopy which revealed a rod shaped calculi measuring 5cms x 0.5 cms, lying freely in the bladder. Mechanical transurethral cystolitholapexy was performed for its removal . This rod shaped calculi was found to comprise of wooden pieces. Recovery was uneventful.

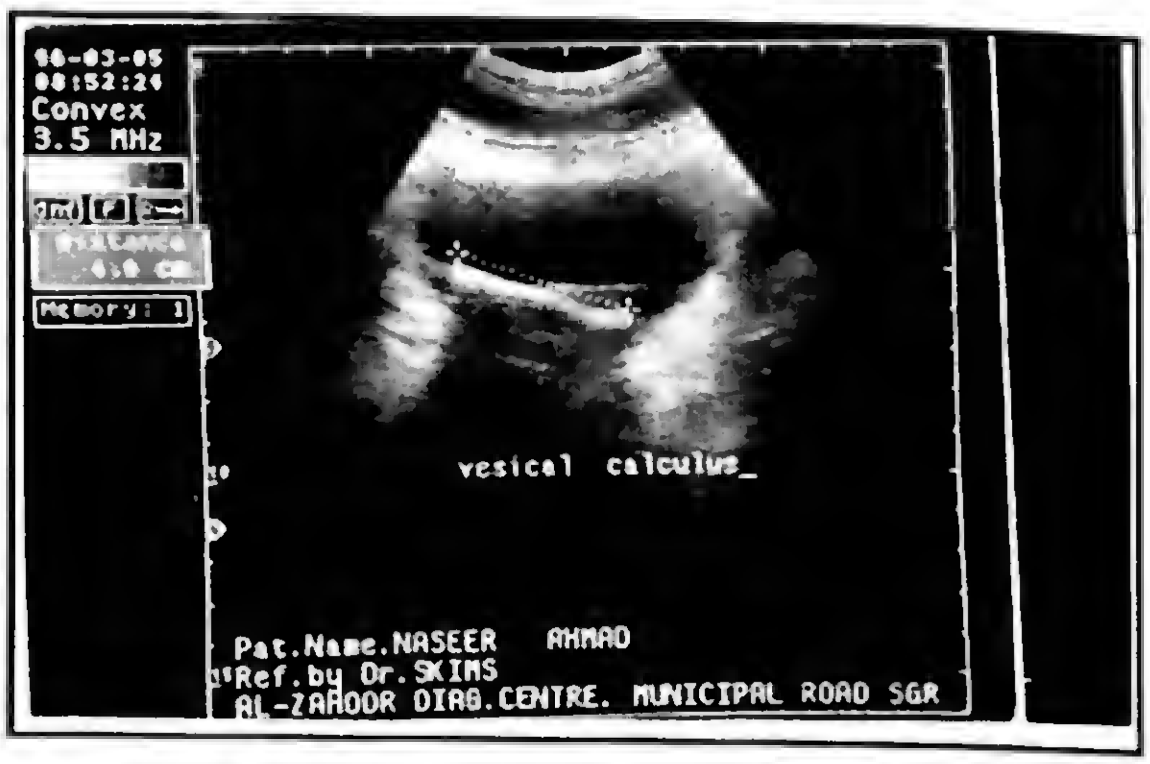

Figure 1. Ultrasonography showing rod shaped vesicle calculi

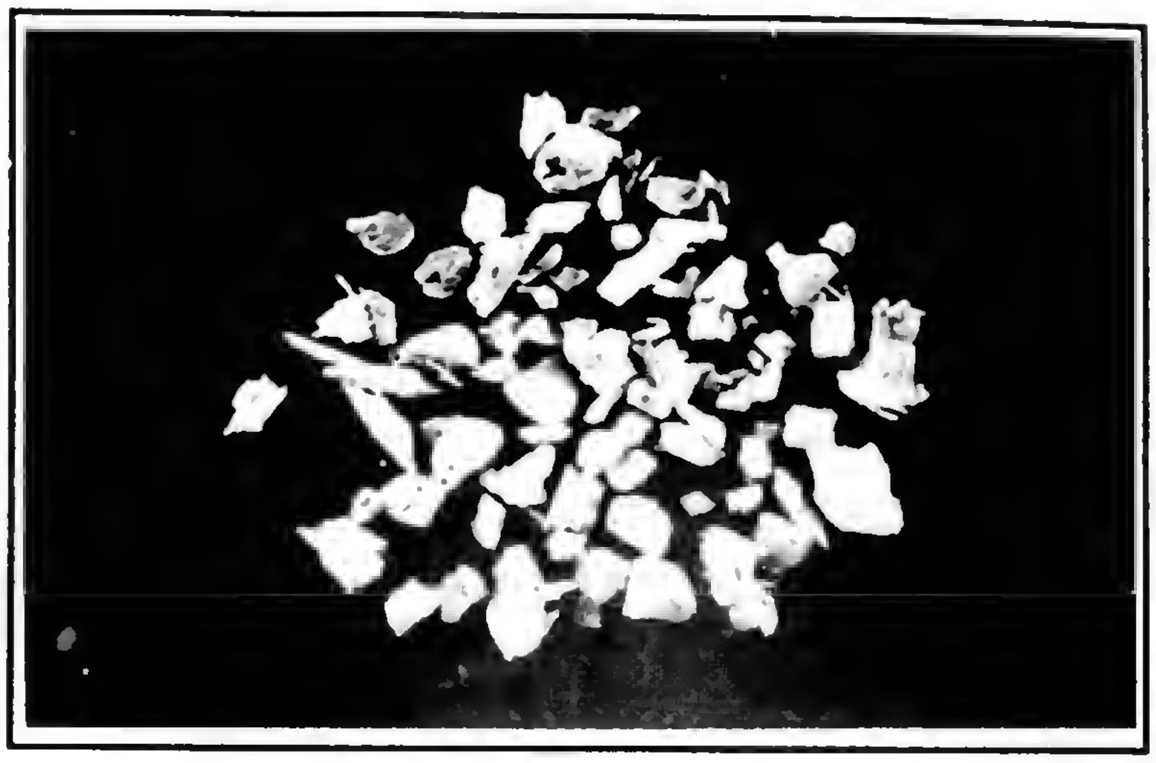

Figure 2. Rod shaped calculi found to comprise of wooden pieces

Reports of transvesical migration or self inserted foreign bodies like surgical

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Key words: Transvesical. Foreign body, Bladder.

sutures[1], metallic hip prosthesis[2] or plastic tube, electric wires, pebbles, urethral dilatation for the purposes of masturbation or curiosity are common[3]. However , reports on the appearance of transvesical foreign bodies following penetration of the rectum are rare[4].

In this case only urine analysis revealed microscopic haematuria at the time of the accident and symptoms took three months to develop. It appears that a sharp piece of wood entered the right perineal region into the rectum, pierced the anterior rectal wall and then entered into the urinary bladder.

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SEASONALITY AND MULTIPLE SCLEROSIS

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ABSTRACT

Multiple sclerosis is a common demylenating disorder with unknown etiology. Psychiatric comorbidity in multiple sclerosis has been studied in detail. Environmental factors as one of the etiological contributors is under debate. We here in discuss the relation of an important environmental factor i.e., Seasonality as one of the contributors to both multiple sclerosis and psychiatric comordibity in the form of seasonal affective disorders.

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INTRODUCTION:

Multiple sclerosis is by for the most frequent of demyelinating disease. The present consensus is that the disease results from an interplay between genetic and environmental factors, resulting in an immunologicaly mediated inflammatory response within the central nervous system.[1] 75% of multiple sclerosis patients suffer from psychiatric morbidity.[2] Intellectual deterioration, abnormalities of mood and personality changes are commonest manifestations.[2] Seasonal pattern labelling is done to affective disorders when there has been regular temporal relationship between onset of major depressive episode and particular time of year.[3] Such pattern of mood disorders is quiet common in our part of world as revealed by pioneering study by Margoob, and Dutta.[4]

CASE REPORT:

A 65 yeas old woman was attending the Department of psyciatry for treatment of Seasonal Affective Disorder from past 4 years. She had recurrent spring-summer depression. The most recent episode of depression was being evaluated by the first author when he noted cognitive decline, with a possibility of Pseudo-dementia. 8 weeks after the treatment for recent episode of depression was started she went into remission for major depressive disorder but her cognitive decline continued and infact became more pronounced. Neuro-psychological testing of memory revealed normal digit span testing but severely effected retrieval. Both verbal and non-verbal memory were effected. Concentration, attention and verbal fluency were also impaired.

This elderly lady had been well, till few years back, when she during the month of April started remaining low, slept most of time, will not move out of her house and seemed to forget many of the past events. For these complaints she was seen by to a psychiatrist who diagnosed MDD and put her on Imipramine 75mg. She did not improve but improved soon after Fluoxetine 20mg was introduced. She returned to baseline after 3 months with even memory reaching pre-morbid state. These episodes recurred during the same time of year at least thrice before the present episode but all the times she revealed back to her pre-morbid state. But after she went into remission for present episode the memory deficits did not go.

LAB FINDINGS:

We conducted lab investigation for metabolic profile, renal functions, haematology, liver function tests. They revealed no abnormality.

NEUROIMAGING:

CT scan brain of the patient was reported as: 1) ? Post-viral effect 2) ? Multiple sclerosis and MRI was suggested to settle the issue. T2 weighted MRI revealed many areas of increased signal intensity particularly periventricular, paraventricular and

Key words: multiple sclerosis.seasonal affective disorders

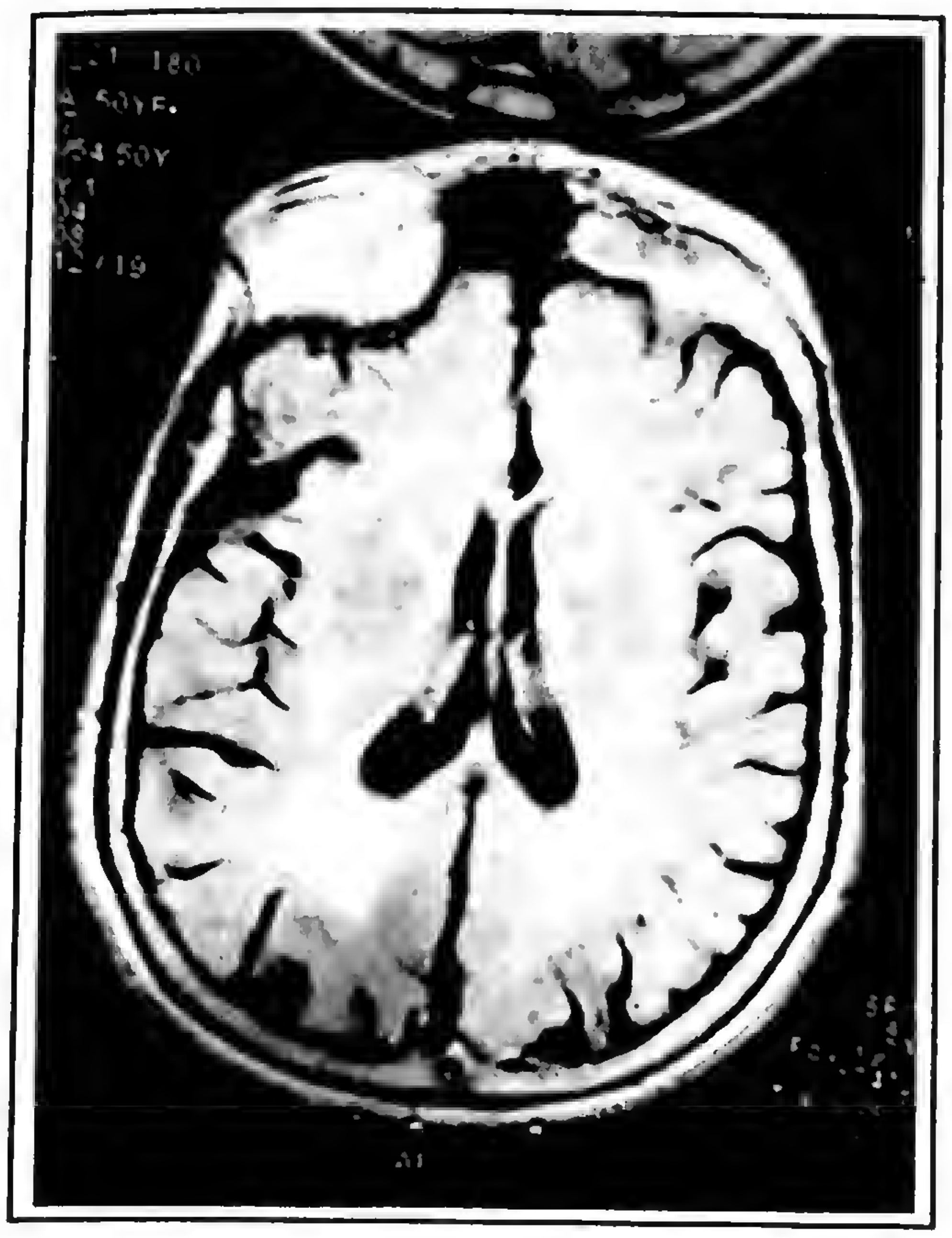

Figure 1

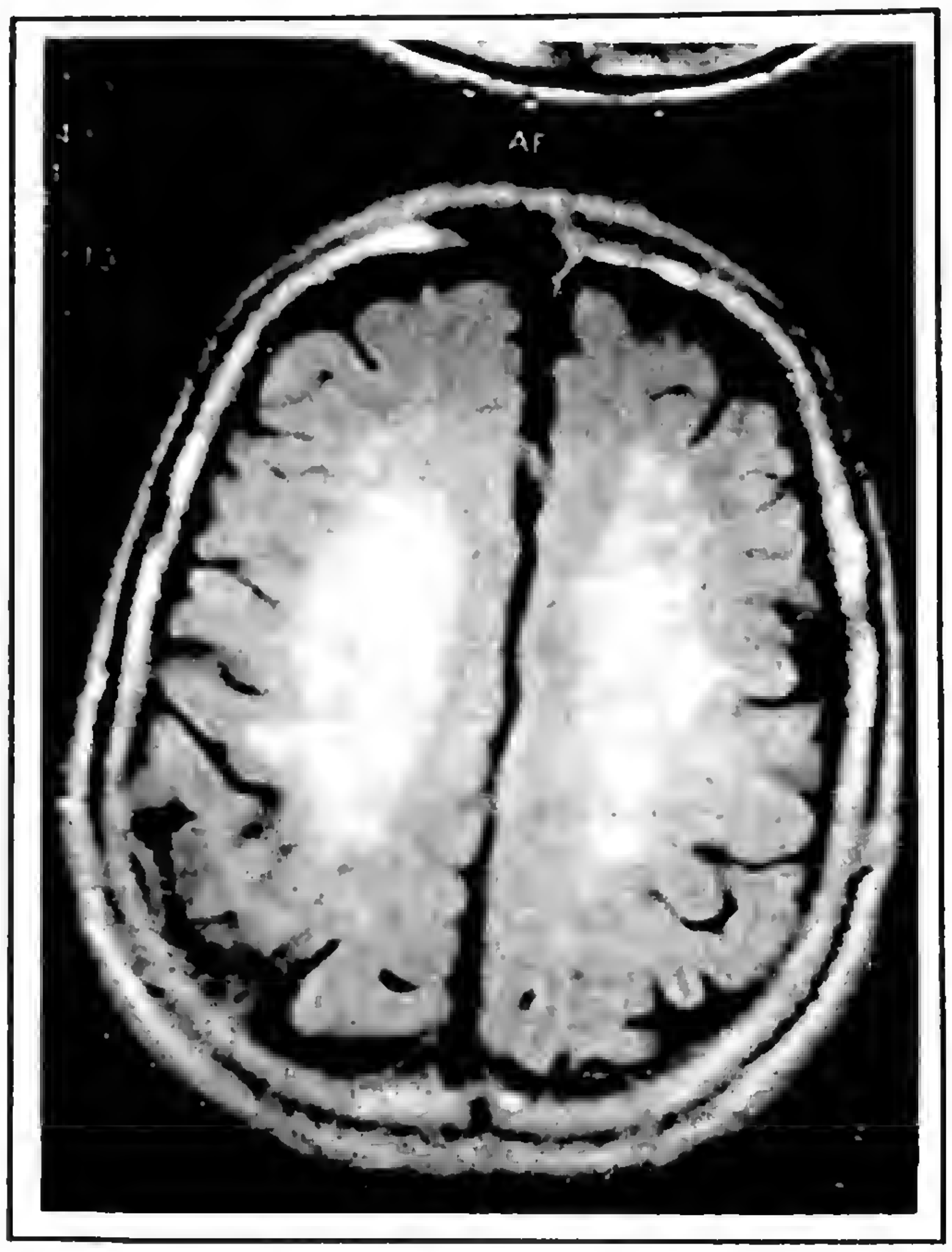

Figure 2

MRI Scans showing increased signal intensity

callosal, most of them greater than 2mm.

DISCUSSION:

Effects of seasonality on multiple sclerosis has not been studied systematically. Apart from few case reports on SAD and multiple sclerosis, Pubmed search reveals no systematic study. Epidemiological evidence similarly points to the importance of the environment, and how living in Southern hemisphere is protective and how protective effect of being black is rapidly eliminated when black persons move to geographical areas of high risk. To date, however, no environmental pathogen has been clearly incriminated.[1] Seasonal ffects may be one of the long list of environmental factors playing their part in the pathogenesis of multiple sclerosis and need to be studied.

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A STUDY OF RECURRENT URINARY TRACT INFECTION AMONG WOMEN ATTENDING OUT PATIENT DEPARTMENT IN S.M.H.S HOSPITAL, SRINAGAR, KASHMIR, INDIA.

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Recurrent Urinary Tract Infection is common among young healthy women, even though they generally have anatomically and physiologically normal urinary tract[1]. Women with Recurrent Urinary Tract Infection have increased susceptibility to vaginal colonization with uropathogens, which is due to greater propensity for uropathogenic E.coli forms to adhere to uroepithelial cells[1].Risk factors for Recurrent Urinary Tract Infection include sexual intercourse, use of spermicidal products, having first UTI at an early age, maternal history of UTI[2].Many factors thought to be risk factors for UTI like pre and post coital voiding pattern, frequency of micturation, wiping pattern and douching have not proved to be risk factors[3].In comparison with the behavioral risk factors for young women, mechanical and physiological factors that effect bladder emptying are strongly associated with Rec. UTI in healthy post menopausal women[4].

In one of our study the total urine cultures received during the year 2001 in the Department Of Microbiology, GMC, Srinagar, Kashmir, were analysed. Out of a total ,550 samples 562 were urine cultures of women.

Our evolving knowledge of long term consequence of UTI centers on the pathogenesis of renal scarring[5]. Having a first UTI at an early age and having a mother with a history of UTI were associated with 2–4 fold increase in risk and were the most strongly associated variable after sexual intercourse[3]. These finding suggest the possibility that inherited factors may be important in some women with Rec. UTI. Urinary tract infections, which are very common in women, are associated with considerable morbidity and recur frequently. The pathogenesis of UTI is very complex and is influenced by many host biological and behavioral factors. We now have a much better understanding of factors that influence the risk of acquiring sporadic and recurrent UTI in women[6]. But there remains much to learn. From our study also risk factors were found to have considerable role to play in occurrence of Rec. UTI in women. E. coli emerged as the commonest organism responsible for causing Rec. UTI. More than 65% of isolates were resistant to newer quinolones like Ciprofloxacin and Norfloxacin, while as to Nalidixic acid 75% of the isolates were resistant. This is contrary to the reports of sensitivity pattern of E. coli isolated from developed countries like USA were 90% of E. coli isolated continued to be sensitive to newer quinolones like Ciprofloxacin. In our study we found that > 80% of E. coli isolates were sensitive to 3rd generation Cephalosporins like Cefixime which correlates with the excellent clinical response shown by patients suffering from UTI to it. Why > 60% of E. coli isolates were found to be resistant to newer quinolones could be explained by over the counter purchase of these drugs in our region leading to increasing spread of resistance among organisms. Though 90 % & 75 % of E. coli isolates continued to be sensitive to Amikacin and Gentamycin respectively they have no bearing on treatment of outpatient UTI. Emergence of resistance during therapy is rare and in uncomplicated acute bacterial cystitis an optimal response is achieved with cure rate in over 95% of women. There is no apparent benefit found by extending the 3 day regime but 5 day regime with betalactams is more effective than three day regime. Recurrent cystitis which occurs during or within first week following treatment suggests treatment failure and should be managed within pre treatment urine culture and antimicrobial susceptibility testing and treatment accordingly with Fluroquinolones or 3rd generation Cephalosporins for 7 days. Later recurrence of cystitis can be managed with short course regimes of antimicrobials as for sporadic infections[1]. History of previous Rec. UTI is a strong risk factor for having subsequent UIT. This could reflect a biological or behavioral predisposition of the host for persistent or recurrent colonization with an uropathogenic strain. Antibacterial characteristics of urine and other host defense mechanism may be an important factor associated with UTI risk but have not been shown clearly to be associated with UTI in healthy person. Sexually active women with risk factors like use of spermicides, diaphragm who have Rec. UTI should be counseled regarding possible association between infection and contraceptive method. Abstinence or a decrease or elimination of the use of spermicide could be expected to reduce the risk of UTI[1]. It is reasonable to suggest to women that early postcoital voiding and more liberal fluid intake with the goal of increasing the frequency of micturation while not shown to be associated with reduced risk might be helpful [1]. Antimicrobial prophylaxis has been demonstrated to be highly effective in reducing the risk of Rec. UTI in women[7,8] and has been advocated in those who experience 2 or more symptomatic UIT over 6 months or 3 or more 12 months period[9] after any existing infection has been eradicated as demonstrated with negative urine culture 1-2 weeks after treatment. There are several alternative approaches to choose from and selection of optimal method of antimicrobial prophylaxis is based on frequency and pattern of recurrence. Prevention of Rec. UTI focuses on detection and treatment in absence of urinary abnormalities to prevent deterioration of renal function.

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POISONING IN CHILDREN

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Poisoning is a Pediatric emergency and a thorough knowledge about the nature and magnitude of problem especially when associated with regional peculiarities is necessary. Pediatric reports [1-8] from various centers reveal the much needed intonation and changing spectrum. This study was conducted in Govt. Hospital for Children, Srinagar, the major referral hospital for pediatrics catering to the whole Kashmir Valley.

During this entire period (4 years), out of 67,59,599 admissions, accidental poisoning accounted for a total of 650 cases (0.96%),out of which 130 cases (0.75%)were in 1997,90 (0.58%)in 1998, 180 (1.2%) in 1999 and 250 (1.25%) in 2000.

Maximum number of cases (49.8%)were in the age group of 1-5 years and least (4.2%) were below 1 year of age. 46% of case were above 4 years of age group the male female ratio was 1.15:1 where as the rural! urban ratio was 1.6

Kerosene oil was the leading poison consumed in all the four comparative years (39.25%) where as food poisoning was the least encountered poisoning (2.4%)

Over all mortality rate was 1 6%.A total of eleven patients died during hospital stay .Highest number of deaths were in 1997 (4 out of 130) and lowest in 2000 (2 out of 250 cases).

The incidence of poisoning has shown a considerable variation with reported incidence ranging form 2.0 to 5.1%1-8V,however in our study, the incident is 0.96%.This lesser incidence in the present series is probably due to better awareness of parents keeping away poisonous substance out of the reach of children and better medical facilities and pediatric care being available in the peripheral areas and some patients well managed at catchments area. In the age distribution our findings are in conformity with the retrospective study reported by Buch etal in 19913 trom the children hospital in Srinagar. Incidence was reported as (49.8%) in the age group of 1-5years and 4.2 % below 1 year of age. This is in accordance with the observation of American sub-committee report, they also found majority of the children belonged to the group of 1-3 years. This predilection of age group is related the oral exploration of the environment during this phase of growth with increasing mobility of child during this period.

Kerosene Oil: Remains the commonest household substance involved in accidental ingestion, it accounted for 40.7% of our cases though other studies [7,8], have reported an incidence of 33.7%. 55%. Kerosene oil ingestion results in toxicity of gastrointestinal, respiratory and central nervous system [2,5] Aspiration pneumonia was the commonest complication observed but responded within 1-2 weeks. CNS complications were noted in 25 cases. These cases had good prognosis. There was no mortality in kerosene group.

Pesticide Poisoning has shown an appreciable rise (20.5%) compared with previous reports [7,8] of 4.9 to 9.2%. Organ phosphorus compounds like tick-20 and Finite. (fenitrothium) are increasingly being used for pest control in houses, constituted many cases. Organophosphorus compounds are frequently used in the valley for fruit crops and accounted for more than 5% of cases in our study. Organophosphorus poisoning has increased dramatically over past few years because of easy availability of pesticides especially in rural areas. **Plant Poisoning** Constituted (15.2%) of poisoning cases in our study, of which more than 50% were due to Datura Poisoning and the remaining (6.3%) were due to consumption of wild seeds which were identified as those of Coria ria neplansis .The fruits commonly known as masoori bari are poisonous and were earlier used to make fly poisons and adulterant for sena .The patients present with symptoms typical of tetanus.

All such cases had an uneventful course other than convulsions, being managed conservatively. Buch etal[3] reported plant

poisoning in 13.4% of cases, of which 20% were constituted by wild fiuit. Majority had symptoms typical of tetanus; there was lone
fatality in their study.

Food Poisoning: was encountered in (3.2% }of cases where as earlier studies[1,2,9,12] have reported incidence ranging from 6.6% to 42.3%.This low incidence is probably due to climatic conditions ofthe valley.[1] patients died due to food poisoning in this series. S. Sitaram[9]in their study reported (32.2%) cases of food poisoning where as Buch etal reported 3.9% of cases of poisoning as food poisoning, which was consistent with our study.

Corrosive poisoning: was least common (2.4%) in our series, mostly due to caustic soda. The cases were managed conservatively and recovered without any complications. Buch etal[3] reported corrosive poisoning in (2.7%) cases, mostly due to caustic soda. Poisoning by medication and chemicals have not shown any Perceptible increase unlike in developed countries where they are posing a major threat[10]. In the presentseriesthey constitute 15.5%. In the miscellaneous group commonest poisoning was ingestion of mosquito repellents especially Good knight because of attractive covering. Other peculiar substances were Naphthalene balls, insect killer; Nail polish remover .Buch etae reported that medications and chemicals were responsible for the maximum number of cases (33%). This was definitely higher than that reported in our study. Main reasons being less use of matoclopromides as antiemitic. Of particular interest were cases of favism in contraindication to previous studies of rarity of GFD deficiency in valley. To conclude, keeping drugs out of reach of children, storing the house hold fuel like kerosene safely, providing immediate medical aid when poisoning occurs and last but not least prescribing drugs more carefully will go along way in preventing hospital admissions and mortality .Creation of more and more poison control cells and general awareness about there role, will help to govern the management of effected cases properly. facilitating proper antedates and upto date knowledge about the management.

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WILMS TUMOUR IN A CHILD WITH FACIAL HEMIHYPERTROPHY, LEFT UNDECENDED TESTES AND MALROTATED CONTRALATERAL KIDNEY

The most common primary neoplasm of the kidney in children is classic nephroblastoma (Wilms tumour). Overall risk of Wilms tumour is 1:10,000 live births. First 3-4 years is the greatest risk. Wilms tumour accounts for 5-6% of all childhood malignancies (leaving aside Japanese children in whome the incidence of Wilms tumour is low). A spectrum of congential abnormalities in association with the Wilms tumour include amredia, hemihypertrophy, pigmented nevi, Beckwith Wiedman-syndrome, hemingiomas, pseudohermaphotidsm, hypospidias, cryptorchidism, horse shoe of fused kidney and umbilical hernia.

We report a case of Wilms tumour with facial hemihypertrophy with left undecended testes.

The 18 month old male child was refered to our department in 1995 for chemotherapy for Wilms tumour (Post Operative Chemotherapy). Earlier he was seen in the department of surgery with a swelling in the left flank rapidly increasing in size occupying almost whole of the abdomen with a duration of two months with no other associated symptoms.

USG showed a well defined mass of mixed echogenicity in upper abdomen (more on left side measuring 8.7x10.3 cms) arising from the left Kidney. Plain KUB showed a large mass lesion seen in the left side of abdomen. IVP revealed right malrotated normal sized and functional Kidney. The mass was likely related to the left kidney, the pericalcyceal system was not well visualized, only pelves seen which was compressed, the features being suggestive of renal origin of the mass most likely Wilms tumour.

CT was advised but not done Nephroureetectomy was done. No secondaries or lymphnode involvement seen. Capsule was free. Histopathology report came as Wilms tumour, composed of blastema with tubular differentiation and mesenchyme.

On examination of the patient we found slight hemihypertrophy of the face and left undecended testes. USG showed right functional kidney, no abdominal organomegaly with left tests in the left inguinal canal. CT was done which showed normal abdominal organs and left kidney area replaced by the loops of small gut. Patient was given post-operative chemotherapy (VAC). Patient is coming for follow up for the last seven years and is doing well. He has undergone orchidopexy on 24th April 2003.

Family History: He has siblings, who are healthy and have no abnormality. No history of Wilms tumourin the family.

Wilms tumour with associated hemihypertrophy, congenital anomalies of external genitalia and the syndromic association like WAGR syndrome (Wilms Tumour, Amredia, genitourinary anomalies, mental retardation), Backwith -Wiedmann Syndrome (Viseromegaly, macroglossia, hypoglycemia, hemihypertrophy, umbilical hernia, gigantisin, omphalocele, adrenocortical carcinomas, hepatoblasloma Wilms tumour and intra abdominal neoplasms) is very rate. A cogential defect in the urogenital ridge, the embryonic precursor of kidneys and genitalia may explain the higher incidences of Wilms tumour in external genitalia.

Overall hemihypertrophy was present in 3% of children registered in NWTS (National Wilms Tumour Study) from 1969 to 1985. 27.7% of children with Bilateral Wilms tumour have anomalies in external genitalia while in children with unilateral Wilms tumour the incidence is 2.3%.

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DYSKERATOSIS CONGENITA PRESENTING AS SQUAMOUS CELL CARCINOMA

Dyskeratosis congenita also called, as Zinsser-Cole-Engmann Syundrome is a rare condition, but widely distributed, first described by Zinsser, later by Cole and Engmann, hence the name given. Most of the cases have been seen in male, but partial forms have been seen in females, also[1]

Histologically cutaneous changes are not pathogonomic and are unimpressive. Clinical features include atrophy and pigmentation of the skin, nail dystrophy and oral leucoplakia. Complications of this syndrome are malignancies in areas of leukoplakia, which appear to be high and may prove fatel. MAlignancies can arise from other mucosal surfaces and atrophic skin. Hematological complications can also occur in the form of blood dyscrasias, myeloid aplasia, refractory anaemia or pancytopenia[2]

A 45 year old male product of a non-consanguinous marriage was referred to us for a non healing ulcer on right side of the oral cavity of two years duration. His systemic examination did not reveal any abnormalities. Cutaneous examination revealed reticulate pigmentation on upper and lower extremities, trunk and face. Telangiectasias with atrophy were also noticed, mostly on hands. Nail dystrophy was seen in few nails.

Oral cavity showed patches of leucoplakia, on left side. Right side showed a big indurated ulcer having everted margins covering almost the whole side . Mandibular lymphadenopathy was noticed. They were tender and discrete. Hair and teeth were normal.

Routine investigation, which included Haemogram, X-ray chest, Electrocardiogram, ultrasonography of abdomen ws normal. X-ray skull did not reveal any calcification. Fine needle aspiration of lymph nodes showed secondary deposits.

Biospy of the lesion revealed well differentiated squamous cell carcinoma. Diagnosis of Dyskeratosis congenita with squamous cell carcinoma was made.

Dyskeratosis congenita also known, as Zinsser Cole Engman Syndrome is a rare but widely distributed disorder, mostly determined by an X-linked recessive gene, however autosomal dominant inheritance has also occurred[3]

The essential features of syndrome include poikilodermatous cutaneous changes, nail dystrophy and oral leucoplakia. Nail changes are usually first to appear,which become dystrophic and may be completely destroyed with occasional episodes of supportive paronychia[4]

Pigmentation of skin is fine, reticulate, grey-brown mostly on neck, thighs and trunk. Atrophy with telangiectasis is also seen. Mucous membrane lesion may follow or coincide with cutaneous and nail changes. It may start as small erosions, succeeded by irregular patches of leucoplakia. Oral genital, ocular and anorectal mucous membranes can get involved. Incidence of malignancy in areas of leucoplakia appears to be high and may prove fatal. Hematological abnormalities include blood dyscrasias, myeloid aplasia refractory anaemia or pancytopenia. Resulting infection or hemorrhage is an important cause of death[5]

Our patient was of 45 years of age having nearly all the characteristic features of dyskeratosis congenita who had developed squamous cell carcinoma. We report this cse because of its rarity and it is worth high lightening that patient having dyskeratosis congenita should be watched to detect early malignancy.

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HEPATOPROTECTIVE ACTIVITY OF ECLIPTA ALBA HASSK. AGAINST PARACETAMOL INDUCED HEPATOCELLULAR DAMAGE IN MICE.

Nahid Tabassum, Shyam. S. Agrawal.

ABSTRACT

The effect of Eclipta alba (EA)extract was studied on paracetamol induced hepatic damage in mice.Treatment with 50% ethanol extract of E.alba (100&250mg/100g body weight) was found to protect the the mice from hepato-toxic action of paracetamol as evidenced by significant reduction in the elevated serum transaminase levels. Histopathological studies showed marked reduction in fatty degeneration and centrizonal necrosis,in animals receiving different doses of E.alba along with paracetamol as compared to the control group.

The mice administered Liv-52,used for comparative evaluation,showed a significant reduction in serum enzyme activity and normal livers.It is stipulated that the extract treated groups were partially protected from hepatocellular damage caused by paracetamol.

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INTRODUCTION:

Eclipta alba Hassk. (Bhringaraja, Fam :Compositae) is a perrenial shrub which grows widely in moist tropical countries.Different uses have been reported for this shrub.It is used as alterative, anthelmintic, expectorant, antipyretic, antiasthmatic, tonic, deobstruent in hepatic and spleen enlargement,in skin diseases and as a substitute for Taraxacum(a popular liver tonic)[1,2]. It is good for the diseases of spleen, stomatitis , toothache, hemicrania, fever, pain in liver and cures vertigo (Yunani). Its juice in combination with honey is administered for Catarrh and Jaundice[1] (Chopra, 1996). In Gujarat district and Punjab,it is used externally for ulcers and as an antiseptic for wounds in cattle. Recently Chandra, 1987[3], have observed a significant anti-inflammatory activity of the powder in rats.It has been reported to be useful in liver ailments[4] (Handa,1986) & has been shown to possess hepatoprotective activity against carbon- tetrachloride induced liver cell damage in animals[5]. But systematic research on any possible effect of E-alba on paracetamol induced hepatotoxicity seems to be scarce. In the present study, 50% enhanol extract of the whole plant was screened for hepatoptotective activity in mice using paracetamol as hepatotoxin. Liv-52 syrup was used for comparative evaluation.

MATERIAL AND METHODS

Eclipta alba (EA) was purchased from a local market in Delhi and identified at the Central Council of Research in Unani medicine.The coarsely powdered drug was extracted with 50% ethanol by cold maceration (I.P 1985)[6]. The solvent was removed at low temperature & reduced pressure and extract stored in a refrigerator prior to pharmacological studies.The extract yield was 13.2% (w/w) in terms of starting material.The dried mass of the extract was macerated with 1% gum acacia & suspended in distilled water to be given orally with a catheter (EA 100 and 250 mg/100g).

Animals and exposure conditions

Healthy albino mice (15 to 30 g) of either sex were housed under uniform husbandry conditions and given pelleted diet (Lipton's India Ltd.)and water ad-libitum.The animals were housed at a temperature of 25 C +-1 C with a 12 hr light /dark cycle.

Paracetamol induced hepatocellular damage.

Mice were randomly divided into five Groups of 8 mice each. Group I served as normal control and received 1% gum acacia suspension only.All other Groups received paracetamol once (500 mg/ kg, p.o, aqueous solution)[7] with Group II serving as paracetamol treated control.

48 hr. after paracetamol administration,Groups III & IV also received EA extract 100& 250 mg/100 g respectively & Group V Liv- 52 syrup (Himalaya Drug Company, India ;2ml/100g) p.o, once daily for 5 consecutive days.16 hr.after administration of last dose of drugs ,animals were anaesthetized with

Key words: Eclipta alba , Liv-52 , Paracetamol , Hepatoprotective .

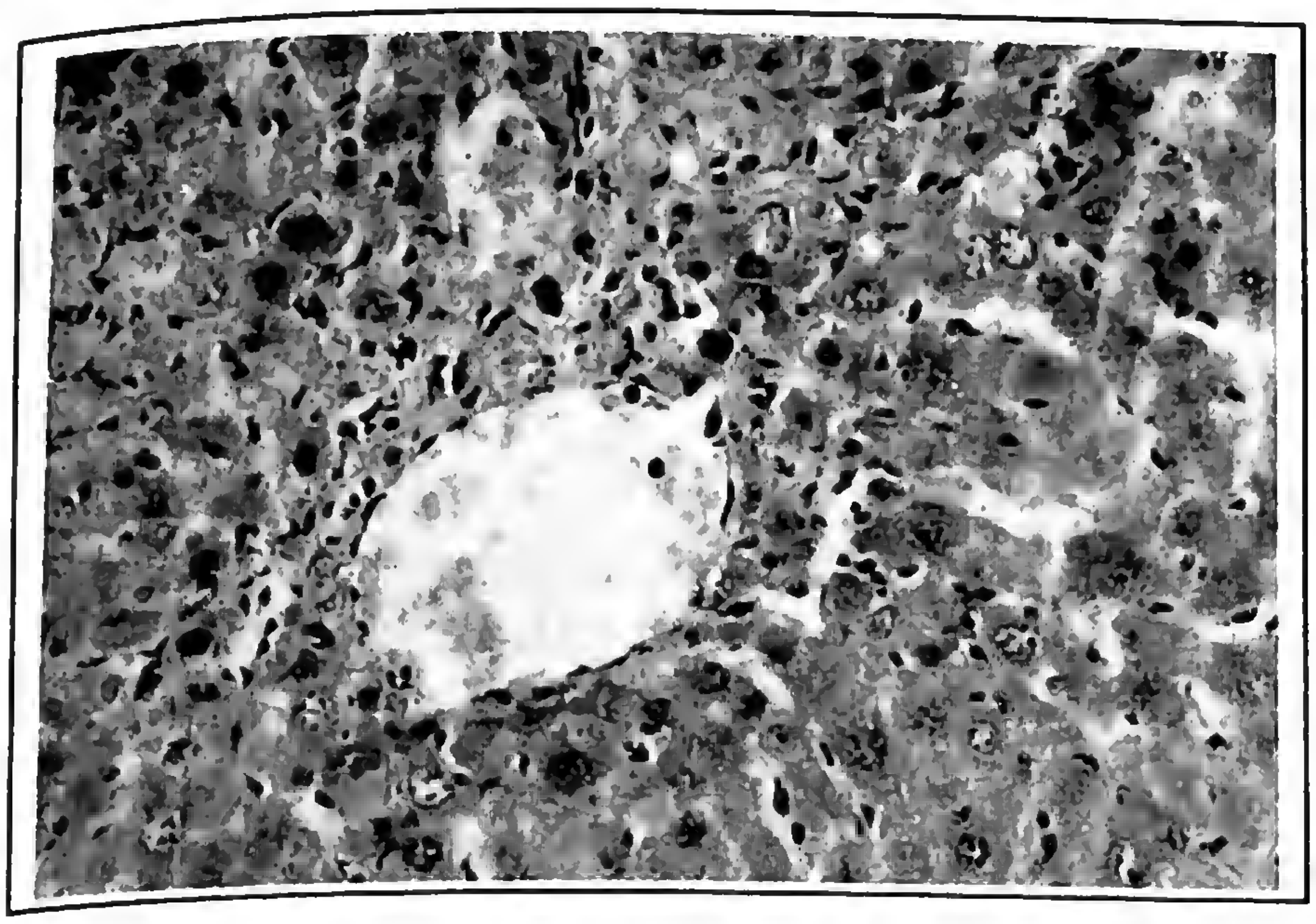

Fig. 1. Centrizonal necrosis after administration of single dose of paracetomol (500mg /kg) (H x E x 400)

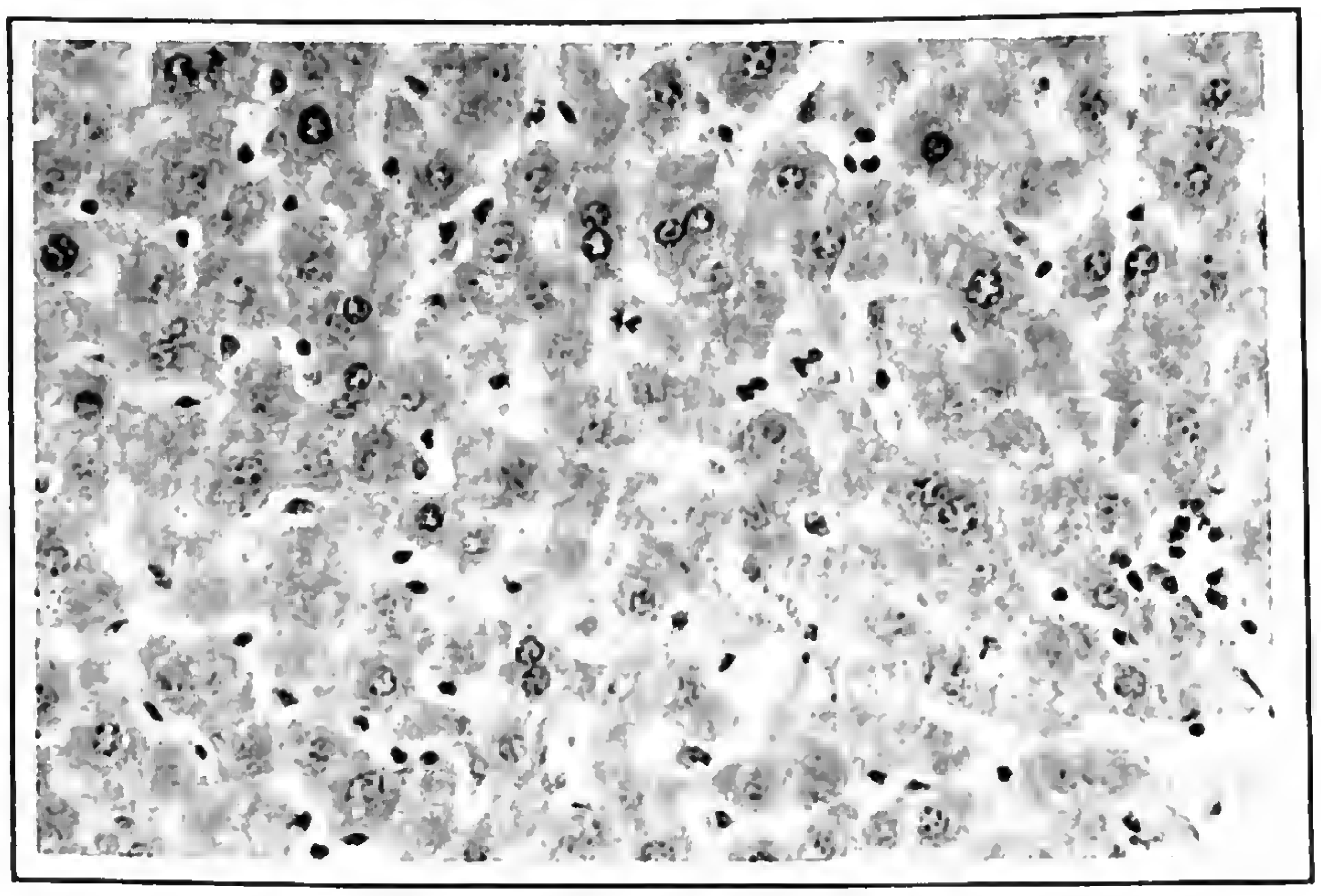

Fig. 2. Binucleate cells, anisonucleosis and sinusoidal dilation after administration of paracetomol (500mg/kg) + E.alba (100 mg / 100g/day) HxEx400)

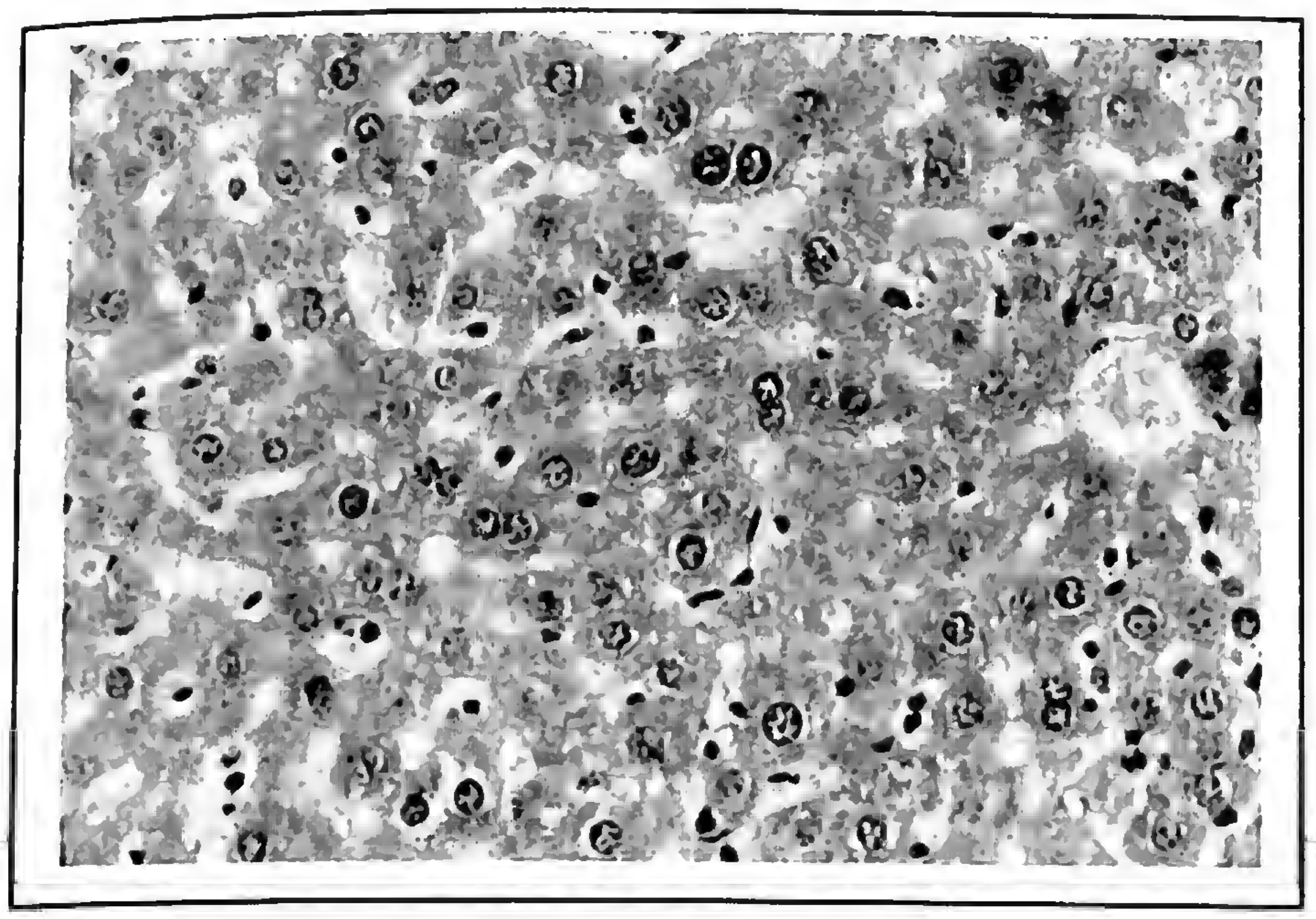

Fig. 3. Binucleate cells spread all over and slight fatty changes with paracetomol (500mg /kg) + E.alba (250mg/100g/day) (HxEx100)

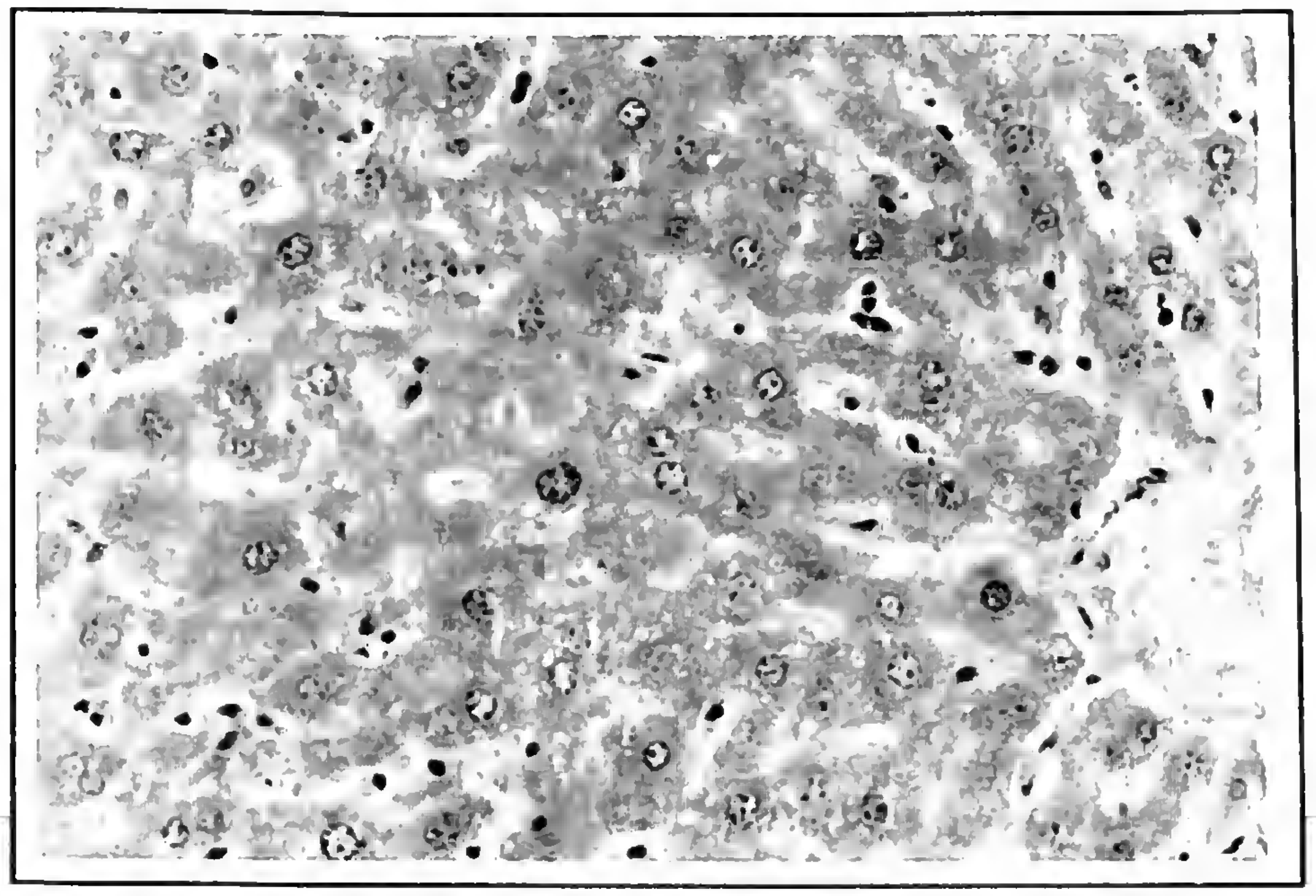

Fig. 4. Normal liver after administration of paracetomol (500mg/kg) + LIV-52 (2ml / 100g/day) (H x E x 400)

ether and blood was collected from the retino- bulbar venous plexus and serum was separated by centrifugation.The serum was then estimated for alanine amino- transferase (ALT) levels[8], which has been shown to be elevated by paracetamol[9]. Mice were killed, livers excised, rinsed clean in saline and preserved in 10% formalin for histopathological study [using 5 micrometer thick sections stained with haematoxylin eosin, (H&E)].Results were statistically analysed using student's 't' test.

RESULTS

Table shows that serum ALT levels were significantly higher in animals receiving paracetamol and reduced significantly in III & IV Groupswhich received paracetamol & EA. The values returned to normal in animals of Group IV receiving 250mg/100gof EA along with paracetamol. Liv-52, which was used for comparative evaluation, produced a highly significant ($p< 0.01$) fall in the enzyme levels.

Histopathological studies revealed centrizonal and focal necrosis and ballooning in livers of mice challenged with paracetamol (Fig 1). But only mild ballooning with sinusoidal dilatation and binucleate cells was observed in Group III, treated with EA (100mg/100g per day) (Fig2) while binucleate cells spread throughout the liver sections and slight fatty changes were observed at the dose of 250mg/100g/day of EA (Fig3). 50% of the livers in Group IV were normal. The livers treated with Liv-52 syrup appeared to be normal as in Group I (Fig 4).

DISCUSSION

Paracetamol causes acute centrilobular hepatic necrosis in rats, mice, guinea pigs, hamsters , rabbits, cats, dogs and pigs[10]. Mice and hamsters are very sensitive while rat is very resistant[11] & in present study, mice were chosen. Only serum ALT levels were estimated as it is the more specific index of liver cell damage[12]. Centrizonal haemorrhagic necrosis is the characteristic lesion in humans[13] and in experimental animals[14]. In the present investigation it was observed that serum ALT levels were significantly reduced in animals receiving EA and paracetamol than those given paracetamol alone indicating that the degree of hepatic cell damage [illegible]

EFFECT OF 50% ETHANOLIC EXTRACT OF E.ALBA AND LIV-52 ON ALANINE AMINO TRANSFERASE (ALT) LEVELS AGAINST PARACETAMOL INDUCED LIVER CELL DAMAGE IN MICE.

	GROUP	ALT LEVELS IU/L	STATISTICALLY Compared groups
I.	1% gum acacia Control	35.09±3.91 (n = 6)	
II.	Paracetamol (500 mg/kg)	50.31±6.81 (n =6)	II Vs I p > 0.05
III.	Paracetamol (500 mg/kg) + Liv-52 (2ml / 100g/day)	31.82±2.78* (n = 6)	III Vs II p < 0.05
IV.	Paracetamol (500 mg/kg) + E.alba (100mg/100g/day)	41.01±6.82 (n = 6)	IV Vs II p > 0.05
V.	Paracetamol (500 mg/kg) + E.alba (250mg/100g/day)	34.62+3.86 (n = 5)	V Vs II p > 0.05

Paracetamol administered in a single oral dose of 500mg/Kg.48 hours before administration of E.ALBA and LIV-52.

lesser magnitude in treated Groups. EA (100 and 250mg/100gm/day) has been found to reduce serum ALT levels in a dose dependent manner (18.4% and 31.18% fall, respectively) and with the latter dose the values returned to normal levels (Table).

The attributivity of the observed alterations of serum ALT levels to hepatic damage on health was confirmed by histopathological studies of liver which have shown that livers challenged with paracetamol have centrizonal necrosis,focal necrosis and ballooning. In animals treated with EA there was no noticeable hepatocellular necrosis. Only mild ballooning & binucleate cells were observed in animals treated with 100mg /g /day of EA while binuclear cells were seen spread all over at the dose of 250mg/100g /day of EA (Fig 2 &3). Binucleate cells in liver are indication of hepatic cell regeneration.

These observations point towards a hepatoprotective activity of EA in the experimental model. Liv-52 syrup, claimed to be a hepatoprotective agent[15] was found to be more effective as hepatoprotective compared to EA as evidenced by both biochemical (38% fall in ALT levels) and histopathological (normal livers) studies.

The results of this study are in corroboration with the earlier reports on the hepatoprotective activity of EA against allyl alcohol induced hepatic necrosis in rats[16] and carbon-tetrachloride induced hepatotoxicity in guinea pigs[5] and rationalise its use as a constituent of various herbal hepatoprotective formulations.

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POSTMENOPAUSAL OSTEOPOROSIS

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Osteoporosis meaning porous bones characterized by low bone mass and structural deterioration of bone tissue. It is common ailment seen in postmenopausal women, resulting in fragile and weak bones highly susceptible to fractures of hips, spine and wrist. One in three women over age of 50 years will develop the disease during their lifetime. Loss of 20% bone mass in 5 to 7 years following menopause is seen. Osteoporosis can be fatal and more women die of hip fractures , than from cancer of ovaries, cervix and uterus combined. It is a silent disease, because bone loss occurs without symptoms.

GENETIC INFLUENCE:

Like other complex diseases postmenopausal osteoporosis have strong genetic influence. DNA analysis is a powerful tool in diagnostics of those woman who are at risk of disease, in identifying potential drug targets, and in predicting response to treatment. The genome searches are making efforts to identify the responsible gene variant and should identify the chromosome containing disease gene, which is a challenge in determining genetic role . Probably hundreds of genes each play a role in bone metabolism, only few of these show genetic contribution to osteoporosis .

BMD: (BONE MINERAL DENSITY)

It detects osteoporosis before fracture occurs, predicts fracture chances in future, detects rate of bone loss ,and monitors effect of treatment. The bone density value at any point in time is a combined function of one 's peak bone mass and the amount of bone loss since skeletal maturation. A low bone density value in a very elderly woman is likely due to progressive bone loss over many years since menopause. In this process bone mass is reduced . and bone quality or architecture also deteriorates . adding further to skeletal fragility. Low bone mass in a young healthy menopausal woman may be due ,in large part to entering menopause with low peak bone mass . The hip BMD is best predictor of hip fractures .Endocrinologist's recommend first measurement at hip.

QUALITY OF LIFE :

This was the theme of the world osteoporosis day 2003. Fragility fractures severely affect the quality of life in postmenopausal woman, especially the spine, vertebral and hip fractures which cause long term disability, associated with high mortality rate among elderly postmenopausal females. The emphasis was laid in preventing the osteoporotic fractures to maintain independent and active life in old age.

A multinational study was done in UK, Italy ,Spain and Germany where it was found that in 95% of the cases , orthopedic surgeons failed to investigate osteoporosis as a cause of fracture .This led to the definition of osteporotic fractures and guidelines for their treatment. Now it is clear that in elderly postmenopausal cases the fractures of hip, spine, wrist, pelvis ,ankle, knee, shoulder and clavicle should be considered and treated as osteoporotic fractures. Studies show that 50 % of females will experience an osteoporotic fracture in their life time, with risk of subsequent fracture as high as five fold. Postmenopausal osteoporotic fractures will increase morbidity and mortality .especially the hip fractures will result in long term disability and even death.

OSTEOPOROTIC FRACTURE RISK OF FEMALES AT 50 YEARS OF AGE :

One-in-three woman over 50 years of age will experience osteoporotic fractures, 1.5 million fractures occurs each year as a result of osteoporosis.

- Hip fractures, woman one-in-six (17.5%)
- Risk fractures , woman one-in-six(16%)
- Vertebral fractures , woman one-in-six (16%)

Risk factors of osteoporosis which are changeable:

1. LOW CALCIUM OR VITAMIN D IN DIET :

If one has low calcium diet over the years , especially during growth years , risk of developing osteoporosis is very high. Its because calcium deficiency leads to decrease in bone formation. Vitamin D is also essential to help the body absorb calcium and maintain bone.

2. LACK OF REGULAR EXERCISE :

Exercise helps to delay osteoporosis. Lack of daily exercise makes one ,vulnerable to osteoporosis, because walking and exercise stimulates bone cells to activity and produce stronger bone. Without activity bones become less dense and weak.

3. CIGARETTE SMOKING :

Smoking doubles the risk factor of osteoporosis as it lowers the estrogen level in blood.

4. UNDERWEIGHT WOMAN:

Woman who are underweight for their height, because of less production of estrogens are also more prone for developing osteoporosis as compared to overweight females who have less chances for the same.

5. USE OF CERTAIN MEDICATIONS:

Drugs like cortisone used for long term in high doses in case of asthma, lung disease, arthritis and allergies can also cause increase risk of developing osteoporosis. Thyroid medications in high doses can contribute to osteoporosis.

6. CHRONIC ALCOHOLICS :

This in absence of liver disease induces osteopenia with low turn-over and increased osteoclast number, resulting in bone loss and calcium infusion from bone into plasma.

NON-CHANGEABLE RISK FACTORS FOR OSTEOPOROSIS:

- Menopause.
- Elderly females (an 80 year old woman is at much higher risk than younger woman with same BMD).
- Genetic influence (family member with osteoporosis).
- Hysterectomy with ovary removal.
- Race (Asian ,next following are African's and American's).
- Medical problems (certain medical problems can increase risk of developing osteoporosis e.g. rheumatoid arthritis, emphysema,chronic bronchitis, hyperthyroidism ,chronic liver disease, intestinal disease).

OSTEOPOROTIC SPINAL AND VERTEBRAL FRACTURES:

These in postmenopausal woman pose a definite problem. It occurs when a compression force is applied to the spine e.g, putting a load on out stretched arms, picking up a heavy grocery bag, lifting a child, other causes are horse riding , or riding in a bouncing boat.

Such fractures can be confirmed by anterioposterior and lateral X-ray of involved area of spine and pelvis bone scan can show a new or previously healed break. Vertebral compression causes loss of height by several inches, spinal khyposis, protuberant abdomen ,restrictive pulmonary disease, stooped posture. Even one compression fracture weakens the spine.

In elderly postmenopausal osteoporotic vertebral fractures ,the orthopedic surgeon can best guide and treat such patients. Nonsteroidal analgesic is given to relieve pain. If narcotics are added, careful dosing and observation is must. Positioning of patient is important, sometimes temporary light weight braces are used to stabilize the spine, which prevents movement so causes pain relief. Symptomatic relief of pain can be given by ice massage used as local anaesthetic during acute pain and moist heat applied every few hours to relieve muscle spasm. Bed rest no longer than one week to avoid further bone loss from immobility. Spinal vertebral fractures heal within 4 to 6 weeks, as capacity to heal remains normal in osteoporosis. Treatment of under lying osteoporosis is an important part of management of vertebral compression fractures.

PREVENTION:

Improving calcium nutrition, vitamin D intake, regular exercise program, hormonal replacement therapy is very essential and should be started in time, calcitonin to prevent further fractures, no smoking and moderate alcohol intake.

In study of postmenopausal woman calcium intake of 1 gram per day appears to be necessary to effect a positive impact of exercise on bone mineral density in spine. Study show that intermittent cyclical treatment with etidronate disodium (HEBP) and calcium plus alphacalcidol may be effective for increasing BMD and preventing fractures in postmenopausal osteoporosis.

TREATMENT:

Treating of postmenopausal osteoporosis should be made in conjunction with patients age, BMD results ,history of previous fractures, high risk factor for bone loss.

In conservative management high doses of calcium intake with exercise program would be continued without any osteoporotic drug and to repeat a BMD test after 2 years. If evidence of bone loss is seen on repeat test, antiresorptive medication should be considered. Some patients with keen personal health beliefs, who are very much concerned about skeletal status, and wanting to stay active and fracture free, take and prefer medical therapy at initial stage only. It keeps them anxiety free and allows participation in all activities. Either plan is appropriate depending on quality of life related issues, objectives and concerns.

It is easier to prevent osteoporosis than to treat it. Best is to retard menopause associated bone loss.

- Estrogens : decrease bone loss by decreasing bone absorption .HRT thought to work best during first 5 to 10 years of menopause , requires commitment to long term use because when therapy stops significant bone loss resumes.

Despite its advantages , 75% discontinuation rate is seen after 6 months . Recommended dosage is 0.625milligram premarin (conjugate estrogen) shown to preserve bone . Stopping of drug is because of concern about venous thromboembolism , with slight increase risk of breast cancer .

· Bisphosphonates: Non hormonal drug used to inhibit osteoclast activity so decreasing bone resorption, with no adverse effect on breast and uterus and no venous thromboembolism . Two oral bisphosphonates have been approved to prevent postmenopausal osteoporosis.

1. Alendronate (Fosamax)
2. Risedronate.

These drugs have shown to increase vertebral and hip BMD, and decrease vertebral fracture risk. Daily dose of 5 mg per day or once weekly is as effective as daily dosage formulation.

· SERMS (selective estrogen receptor modulator)

These estrogen like compounds have antiresorptive properties. Raloxifene increase BMD in spine ,hip and wrist athough to a lesser extent than HRT/ERT or Bisphosphonates . Like estrogens Raloxifene has potentially harmful effects like VTE, but unlike estrogens raloxifene does not jeopardize endometrial/breast tissue. It does not ease menopause symptoms , but may exacerabate hot flushes.

CONCLUSION:

· ERT considered good choice for women who need therapy for other postmenopausal symptoms. Raloxifene considered for women who do not have troublesome vasomotor symptoms and want a medication that improves BMD without risk to breast and uterus . Bisphosphonates are excellent for women who need to prevent bone loss only.

Barring about drug selection. clinicians should recommend adequate intake of calcium (1200 to 1500.mg per day) and vitamin D (400 to 600 IU per day) and resistant type exercises to augment the drug benefit . Interventions to Stave off bone loss can help to improve postmenopausal women quality of life and avoid serious consequences of fracture . Clinicians should take lead in prevention strategies that can increase BMD and decrease fracture risk. "Medical experts agree that osteoporosis is highly preventable".

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JK-PRACTITIONER

A STUDY ON "DISEASE PREVALENCE" IN LADAKH, JAMMU AND KASHMIR

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ABSTRACT

Governments and international organizations have widely recognized the need to improve the health of the poor. In the 1970's, WHO led a global effort to achieve "Health for All" by the year 2000. Representatives from more than 130 governments in 1978 signed "Alma-Ata Declaration" stating that inequality in the health status of the people is politically, socially and economically unacceptable. Though more than 25 years have passed since the Almá-Ata Declaration, but "Health for All" remains an elusive goal and health disparities between poor and rich countries are growing. Knowledge bout the prevalence of various diseases and their causes can help the governments address the burden of diseases in a rational manner. Though a lot of research has been conducted to estimate the prevalence of ailments and their causes in the world but such an exercise has not been conducted in Jammu and Kashmir. The objective of this paper is to estimate the prevalence of various diseases by socio economics characteristics in Ladakh Division of Jammu and Kashmir . The survey was conducted in Kargil and Khalisi Blocks of Ladakh Division and information about the prevalence of diseases was collected from 4051 person. The results show that the most common ailment prevalent in the region is arthritis followed by peptic disorders . The study has also shown that the physical environment and socio-economic conditions are associated with the prevalence of diseases . Finally , the low prevalence of some ailments like diabetes , TB, heart ailments and mental disorders need further exploration.

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INTRODUCTION

The 20th century witnessed a revolution in human wealth and well-being . Average life expectancy at birth has increased in developed countries from around 45 years in 1900 to more than 70 years in 1999 (UN,19766). Less developed countries also enjoined dramatic, albeit less extensive, improvements in living standard and declines in mortality . The sweeping improvements in health and success at controlling such ancient human foes as small pox and cholera created expectations that everyone could attain good health.

As some health threats have receded, however, other threats have emerged such as HIV/AIDs and new cancer causing substances. Some disease- causing microbes have become resistant to medicines commonly used to treat them. Aspects of modern life appear to encourage unhealthy behaviour , such as smoking , drug addiction and high fat diets. Besides there is a substantial gap in mortality and disability among and within countries. A growing recognition of this disparity promoted the World Health Organizations to mount an international effort to attain "Health for All" by 2000 . Representatives from more than 130 governments in 1978 signed "Alma-Ata Declaration" stating that inequality in the health status of the people is politically,socially and economically unacceptable (WHO,1978).Though more than 25 years have passed since the Alma-Ata Declaration , but "Health for All" remains an elusive goal (Dara Carr,2004). In the developing countries the leading cause of death still include diseases such as diarrhea , measles and malaria. Large disparities in health persist both within and between countries and the health disparities between poor and rich countries are growing. For example in Africa, infectious and parasitic diseases account for more than half of all deaths in 2001, compared with 2 percent in Europe (WHO,2002) . More than 2.3 million people , primarily in developing countries, die from eight vaccine preventable diseases

Key words: disease.prevalence

annually (Dara Carr, 2004).

In India also there are large disparities in the health status of the people among various states. Infant mortality rate in India ranges from 16 infant deaths per thousand live births in Kerala to more than 86 in Meghalaya, Uttar Pradesh and Madhya Pradesh (IIPS.2000). Similarly , the State variations in the prevalence rate of tuberculosis, Jaundice and asthma are also large. A number of factos contribute to the disparities in the prevalence of disease in a society. High levels of absolute poverty make people in poor societies vulnerable to diseases, because they lack access to safe drinking water, decent housing, adequate sanitation, food education, professional health care, transportation and proper health information.

OBJECTIVES.

Though a lot of research has been conducted all over the world and in India to estimate the prevalence of ailments and their causes but this topic has received very little attention in Jammu and Kashmir . Though some efforts have been made to analyse the incidence of disease in the state , but they have mostly concentrated on Kashmir Valley and Jammu region. Ladakh Division which differs from Jammu and Kashmir regions has been left out from such studies. It is pertinent to mention that Ladakh Division because of its unique location differs widely from the two regions of Jammu and Kashmir geographically, culturally, socially and linguistically and economically , thus providing a fertile ground for research in epidemiology. The objective of this paper is to, therefore, to fill this gap to some extent and estimate the prevalence of various diseases in Ladakh division by socio economic characteristics and demographic characteristics . It is hoped that the present study may help us to identify the emerging health issues of the region so that proper preventive and curative strategies are framed to address the health issues in this part of the world in an efficient manner.

AREA OF STUDY.

Ladakh division has a total area of 96901 Sq. Kms (Digest of Economics and Statistics, 2001-02) which includes 37555 Sq. Kms under the occupation of China . The division consists of two districts namely Leh and Kargil . The average altitude of the region is about 4000-5000 meters above the sea level.Ladakh division is a vast mountainous terriority which extends from Zanaskar in the south to Karokaram, Nun-Kun and Nanga Parbat in the north. The region experiences extreme climatic conditions. Summer are very hot and winter are very sever with mean temperatures touching sub zero level and a minimum temperature of -30 C. The total population of the region in 2001 was 2.25 lacs (Directorate of Census Operations, Jammu and Kashmir, 2001) . Population density is about 2 person per square kilometer and sex ratio is also very low (888 female per 1000 males) . Less than 20 percent of the population live in urban areas and overall literacy is 54 percent. This part of the world remains closed from the rest of the world for almost six months a year and therefore is economically the least developed region of the state. The people of Ladakh are a mixture of Mongoloid and Aryan race and bear a close affinity with the features of the Tibetans. They lead a very hard life . The life of people of is governed by the deep-rooted traditional values and cultural norms. Thus the poverty , topography, extreme climatic conditions and traditional values may be inflicting upon the halth of the people of Ladakh in one way or the other.

METHODOLOGY.

As already mentioned that Ladakh comprises the two districts of Leh and Kargil and both the districts were included in the study. However, from each district only one medical block was selected to estimate the prevalence of diseases. Khalsi block from Leh district and Kargil block from Kargil District were chosen for primary data collection. From each block it was decided to select 5 percent of the total population so as to get fairly reliable estimates of the prevalence of morbidities by various socio economic, demographic, environmental and cultural characteristics. Equal allocation was also given to the urban areas of Kargil districts. Since Khalsi block does not have urban population so the study was restricted to only rural areas of the Khalsi block.

The staff engaged in the survey were trained for three days. This training consisted of class room training, general lectures and demonstration and field practice . The field in Kargil block was conducted by 8 teams and data collection in Khalsi block was undertaken by 4 teams. Each team comprised of one Pharmacist and one Female Multipurpose Health Worker. The data collection activities of two teams each was supervised by a Medical Officer. The main field work was carried out in the month of June, 2003 and the authors personally visited three teams to supervise the data collection activities. A total of 319 households (162 Urban and 157 Rural) were surveyed in Kargil district and information was collected for 2496 household members in these households. Similarly 203 households were contacted in Khalsi block and information about morbidities was collected for 1555 house hold members.

FINDIGS: REFER TABLES AND FIGURES

RECOMMENDATIONS.

This study shall go a long way while formulating health care policies for the people of Ladakh. e.g. while procuring the medicines for the region the diseases prevalent in the area need to be keep in mind and general policy of the state should not be applied here.

More over a team of experts should be framed to identify the root causes of their problem and strategies should be developed to remove the root causes and improve the living conditions living in this part of the world.

Experts from different disciplines need to study in depth why the diseases like , diabetes, malaria ,TB, Carcinomas, heart ailments ,mental disorders etc are less prevalent in this area and in depth study may help to replicate some of the things prevalent in Ladakh in other part of the state and world in the interest of mankind.

Table - 1

FINDINGS

The immunization Survey of children of 0-10 years of age was also done.

SUMMARY REPORT OF DISEASE PREVALENCE SURVEY OF BLOCK KARGIL - DISTRICT KARGIL

1	Total Population of Block	30000	
2	Population to be Surveyed(50 % of Total Population)	1500	
3	Households to be Surveyed	300	
4	Rural Population	750	
	Rural Households	150	
5	Urban Population	750	
	Urban Households	150	
6	**Actual Population Surveyed :**		
	Urban	1302	
	Rural	1194	
	Total	***2496***	
7	**Household Surveyed:**		
	Urban	162	
	Rural	157	
	Total	***319***	
8	**Sex – wise Breakup :**	**Urban**	**Rural**
	Male	680	606
	Female	622	588
	Total	***1302***	***1194***
9	**Age – wise Breakup :**	**Urban**	**Rural**
	1 – 15 yrs of Age	494	431
	16 -29 yrs of Age	387	299
	30 – 44 yrs of Age	198	219
	45 – 59 yrs of Age	134	138
	60 yrs & Above 60 yrs of Age	89	107
	Total	***1302***	***1194***
10	**Religion – wise Breakup:**	**Urban**	**Rural**
	Muslims	1302	938
	Hindus / Sikhs	x	x
	Buddhists	x	256
	Total	***1302***	***1194***
11	**Income – wise Breakup of Households :**	**Urban**	**Rural**
	Up to Rs: 5000 P.M	83	141
	Above 5000 up to 15000 P.M	67	15
	Above 15000 P.M	12	01
	Total	***162***	***157***

Table - 1

DISEASE PREVALENCE BREAKUP(Block Kargil, Distt. Kargil)

S.NO	DISEASE	URBAN	RURAL
1	Arthritis	95	127
2	Carries Tooth	83	52
3	Acute Diarrhea / Dysentery	68	33
4	Hypertension	63	41
5	Tonsillitis	58	12
6	Worm Infection	57	44
7	Anaemia	48	36
8	Rhinitis	28	108
9	Acid Peptic Disorders	24	125
10	Dermatitis	17	33
11	Pharyngitis	11	31
12	Fungal Infection	08	23
13	Bronchitis	07	12
14	Muscular - Skeletal Disorder	07	03
15	Abscess	07	05
16	Br. Asthma	16	22
17	Mental retardation	06	04
18	Sinusitis	05	62
19	Scabies	05	07
20	UTI	03	22
21	Rh Fever / R. Heart Disease	02	15
22	Stroke	02	x
23	Cerebral Palsy	02	01
24	TB	01	01
25	Infective Hepatitis	01	x
26	Pediculosis	01	06
27	Nephritis	01	02
28	Nephrotic Syndrome	01	07
29	Diabetes	01	01
30	ASOM / CSOM	x	37
31	Pyoderma	01	21
32	Bleeding Disorders	x	06
33	Blindness	x	05
34	Dislocation Fracture	02	03
35	Pneumonia	05	17
36	Others	17	63
Total		643	987

Table - 3

SUMMARY REPORT OF DISEASE PREVALENCE SURVEY OF BLOCK KHALSI- DISTRICT LEH

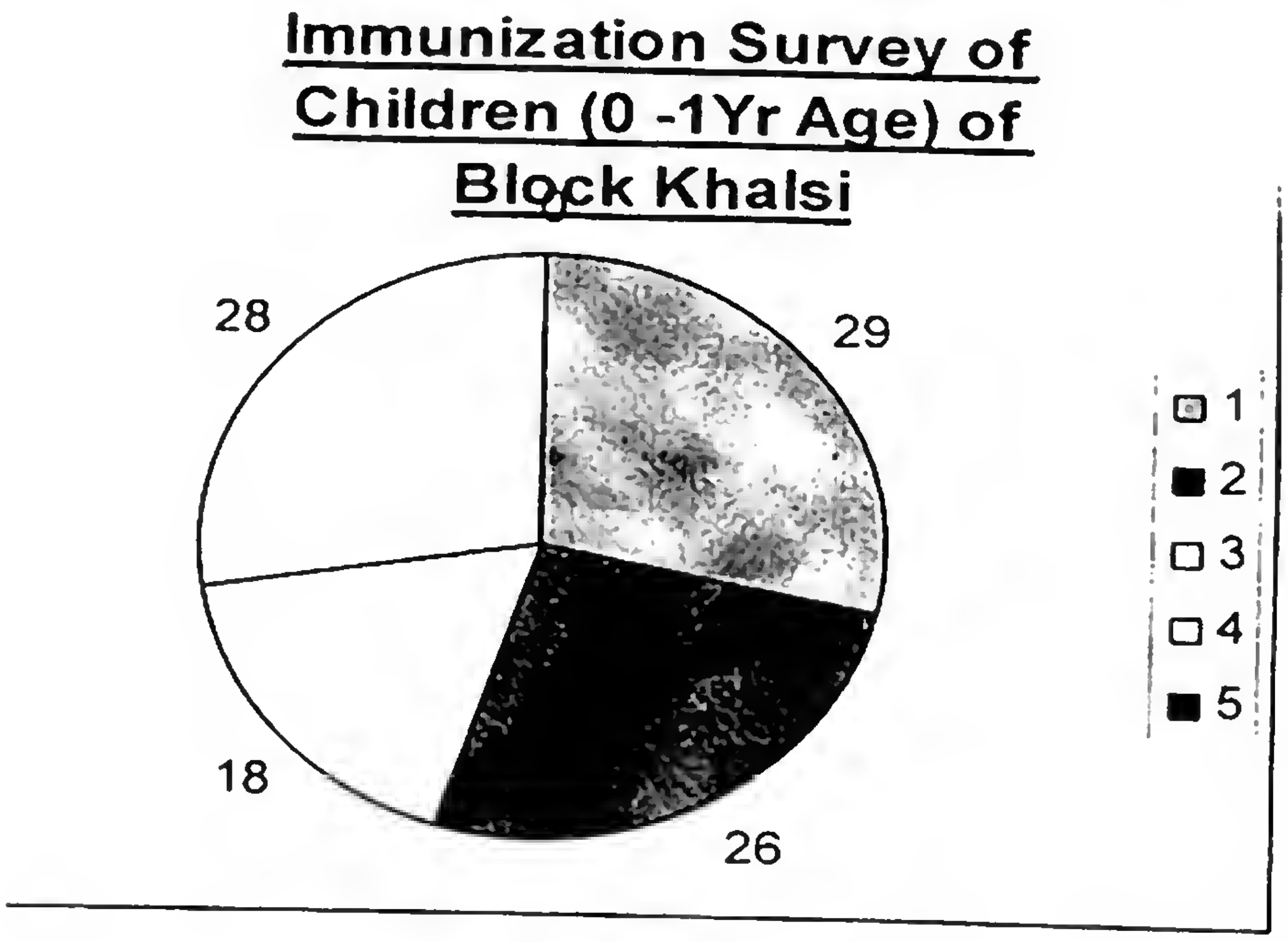
1	Total Population of Block	16156
2	Population to be Surveyed(50 % of Total Population)	808
3	Households to be Surveyed	162
4	Actual Population Surveyed	1555
5	Actual Households Surveyed	203
6	**Sex – wise Breakup :**	
	Male	791
	Female	764
	Total	1555
7	**Age – wise Breakup :**	
	1 – 15 yrs of Age	476
	16 -29 yrs of Age	429
	30 – 44 yrs of Age	298
	45 – 59 yrs of Age	202
	60 yrs & Above 60 yrs of Age	150
	Total	***1555***
08	**Religion – wise Breakup:**	
	Muslims	x
	Hindus	x
	Sikhs	x
	Buddhists	1538
	Christians	17
	Total	***1555***
9	**Income – wise Breakup of Households :**	
	Upto Rs: 5000 P.M	189
	Above 5000 upto 15000 P.M	14
	Above 15000 P.M	x
	Total	***203***

Table - 4

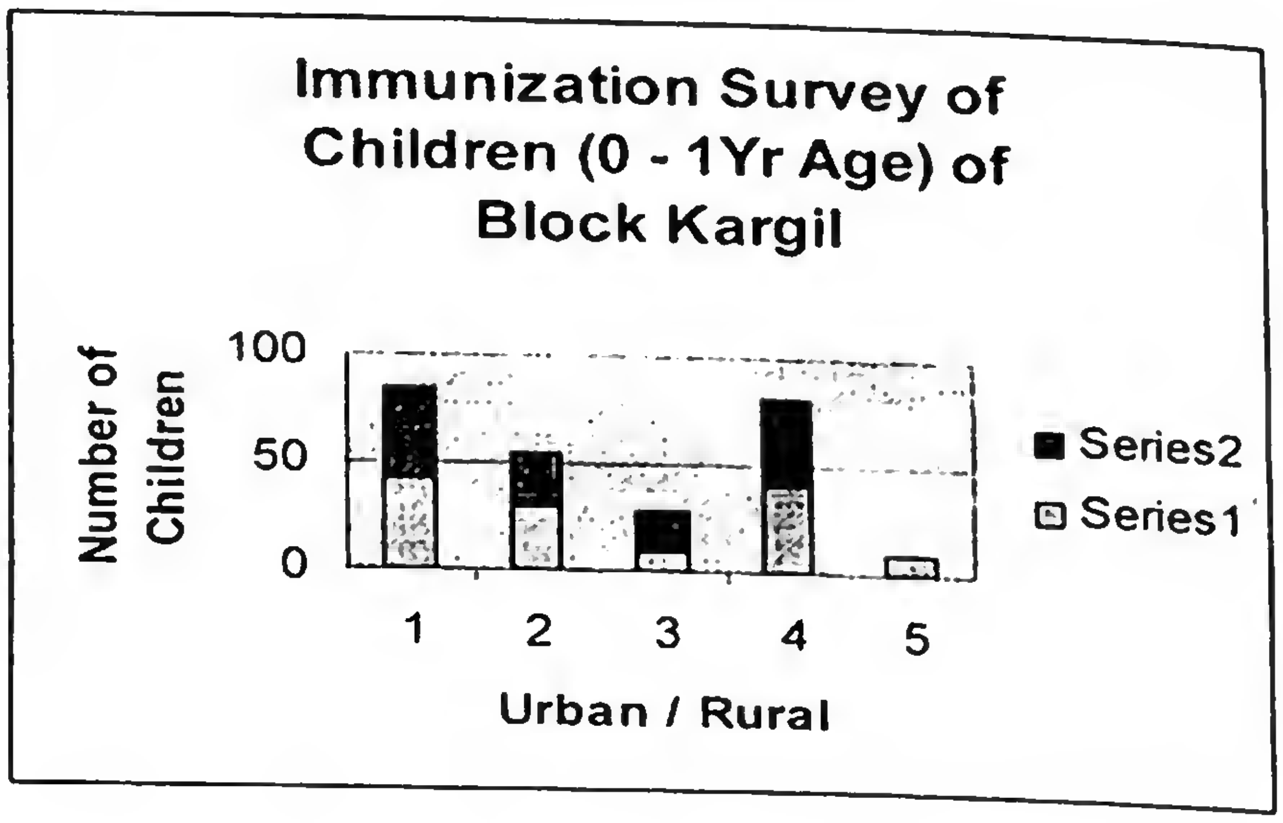
DISEASE PREVALENCE BREAKUP(Block Khalsi District Leh)

1	Arthritis	57 (13%)
2	Carries Tooth	73 (16%)
3	Acute Diarrhea / Dysentery	39 (9%)
4	Hypertension	40(9%)
5	Tonsillitis	4
6	Worm Infection	7(2%)
7	Anaemia	20(4.8%)
8	Rhinitis	25 (5.5%)
9	Acid Peptic Disorders	65 (14.5%)
10	Dermatitis	4
11	Pharyngitis	5
12	Fungal Infection	1
13	Bronchitis	9 (2.3%)
14	Musculo - Skeletal Disorder	10 (2.4%)
15	Abscess	1
16	Br. Asthma	5
17	Mental retardation	6
18	Scabies	2
19	UTI	1
20	Rh Fever / R. Heart Disease	4
21	Cerebral Palsy	2
22	TB	4
23	Nephritis	3
24	Diabetes	1
25	ASOM / CSOM	22(5%)
26	Blindness	1
27	Dislocation Fracture	2
28	Pneumonia	2
29	Epilepsy	2
30	Accidents	3
31	Pregnancy related Disorders	2
32	Burns	1
33	Polio	1
34	Menorragia	1
35	Xeropthalmia	4
36	Others	14
	Total	445

SUMMARY OF IMMUNIZATION SURVEY OF CHILDREN 0-1YR OF AGE OF BLOCK KHALSI AND BLOCK KARGIL



Block Khalsi



Block Kargil

1	Total Children (0-1 yr Age)	29
2	Children who received 3 Doses of Polio & DPT	26
3	Children who received Measles Vaccine	18
4	Children who received BCG	28
5	Children who received 1st Dose of Vit – A	x

		Urban	Rural
1	Total Children (0-1yr Age)	42	43
2	Children who received 3 Doses of Polio / DPT	29	26
3	Children who received Measles Vaccine	10	18
4	Children who received BCG	40	42
5	Children who received 1st Dose of Vit – A	9	x

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DISCOVERY OF HEPATITIS E VIRUS - THE UNTOLD STORY

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COMMENT

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Viral hepatitis is a cause of considerable morbidity and mortality, both from acute and the chronic sequelae. It is a global health problem and breaks all known human barriers in causing disease and suffering. Globally over 850 million are chronic carriers of hepatitis B and C and account for over 2 million deaths per year. However, epidemics of jaundice had been a menace to humanity since antiquity. The first description of viral hepatitis is attributed to Hippocrates (460-375 BC), who described the clinical features of epidemics of jaundice have been feature of many military campaigns and have been determining factor for defeat and victory of historical wars. Epidemic jaundice was thought to be catarrhal in origin. This concept was forwarded by Bamberger (1855) and supported by Virchow (1865). It was postulated that the initial lesion was gastroduodenitis followed by spread of catarrh to the epithelium of the bile ducts, thereby producing an obstructive jaundice. This concept was defeated by studies of Dible (1943), who performed needle biopsies of the liver on patients with epidemic jaundice and proposed hepatocellular damage or "hepatitis" as the underlying cause of epidemic jaundice. The most important human experiments in the history of viral heatitis were that of Krugman et al who distinguished infectious hepatitis from serum hepatitis by the use of transmission studies at the Willowbrook State School in New York, an institution for the mentally retarded, where viral hepatitis was an epidemic disease. This was a conclusive study which could not be repeated today. Blumberg et al (1965) made a breakthrough study when he published his classic paper on Australia antigen. This subsequently led to the discovery of hepatitis B virus. Feinstone et al (1973) visualized hepatitis A virus particles by immune electron microscopy in stool extracts of patients with acute HAV virus infection was quickly controlled. Two groups (Alter et al & Tabor et al) of investigators reported that 90% of post-transfusion hepatitis were of not related HAV & HBV. These were the first indication of an existence of another human hepatitis virus. These two papers gave the concept of non-A, non-B hepatitis. It took a number of years before Choo et al identified hepatitis C virus from post-transfusion non-A, non-B hepatitis and developed serological test for its diagnosis. Hepatitis C virus is of major importance globally in causing chronic hepatitis, cirrhosis and hepato-cellular carcinoma. While all these major discoveries of hepatitis viruses were occuring, the status of epidemic jaundice which had introduced the subject of hepatitis to humanity remained ignored. A number of epidemiological shifts had occured to the epidemic jaundice over the 100 years since it had been described. Epidemics had limited to regions of the developing world with low socio-economic status, bad sanitation and unsafe water supplies. Epidemics of jaundice in Indian subcontinent were reported on regular intervals, involved hundreds and thousands of people with considerable morbidity and mortality. In fact epidemic jaundice was a national health problem in India. An epidemic of jaundice which hit Delhi, the capital of India, in 1955-56 caused estimated

29,300 of jaundice. This epidemic was studied by Indian Council of Medical Research and reported as a classical hepatitis A disease. However, diagnostic tests for hepatitis A virus were not available and done on these sera to confirm or refute the diagnosis.

During this period, I was a DM trainee in Gastroenterology and Hepatology at Postgraduate Institute of Medical Education and Research, Chandigarh, India from June 1976 to June 1978. During this period I was most impressed by some aspects of viral hepatitis in North India. Repeated epidemics of viral hepatitis were reported from number of regions, with high morbidity and mortality. Fulminant hepatitis was seen in high percentage in third trimester pregnant women with high maternal and fetal mortality. Viral hepatitis in pregnant women in the West was not reported to have high incidence or severity. Data from the developing countries were seen with skepticism as bias could not be ruled out from hospital reported data. In fact till that time no well reported field epidemiological study on epidemic hepatitis had been done. Professor D.V. Datta with whom I was most impressed as a researcher during my DM training would call to the Liver laboratory for a cup of strong coffee following the morning meeting and ask me in his typical Punjabi style "Sultan, why do women come with fulminant hepatitis and die." He knew I did not know the answer but yet was eager to find out my response. With these thoughts about viral hepatitis and pregnancy in India deeply engrained in my mind, I returned to Kashmir to practice Gastroenterology as a consultant in Internal Medicine at the Government Medical College Srinagar, Kashmir, India. In November, 1978, a large scale epidemic of jaundice was reported in over 200 villages in District Baramulla of Kashmir valley. A major panic was announced due to magnitude of disease involving young adults and deaths in pregnant women. An opportunity had come for me to define the data clinical duties and responsibilities, visited the epidemic affected area in the next 2 days, and approached the health services for manpower support to do a door to door survey for new cases of jaundice. We were in the field for house to house study within two weeks of the first report of the epidemic. Sixteen affected villages with a population of over 16,000 were identified as the study area. Over the next 6 months each house was visited weekly and all members were examined for possible symptoms and signs of hepatitis. Blood samples were examined for possible and randomly selected non-affected persons for biochemical and virologic studies. A research laboratory was established in the Medical College Campus to receive process and store sera. International support was sort to test sera for hepatitis A and hepatitis B virus infections. Originally 35 sera were tested in Birmingham for HAVand HBV infection. Subsequently a large pool of sera was tested in Netherlands, Japan and USA. Following these preliminary sera analysis, support from Netherlands in the form of kits was received and we performed hepatitis A and hepatitis B in our Medical College laboratory. Concurrent with the field study, Medical College hospital was used to further study admitted patients for clinical presentation and liver histoloty by performing percutaneous needle biopsies of nonfulminant cases and postmortem biopsies of fatal fulminant cases. Results of epidemiological data, virologic studies and histological findings were available in May 1979. Critical analysis of data were remarkable in the conclusions. The data were convincing that (i) the epidemic curve was highly compressed lasting for less than 6 weeks and was of common source type, (ii) the disease was caused by a hepatitis virus, (iii) the agent was spread through contaminated water, (iv) the agent was of non-A, non-B type, (v) epidemic involved young adults with sparing of children (vi) there was high incidence and severity of disease in pregnant women and (vii) liver histology in a subgroup of patients revealed charateristic histological findings. In fact the disease incidence and severity in latter pregnancy was so remarkable that we had difficulty in finding a third trimester pregnant women at the tail of the epidemic disease. We estimated that the epidemic had involved 200 villages wit a population of over 600,000 and had caused icteric disease in 20,000 individuals with 600 deaths. These data were reported to national and international societies and published in American Journal of Medicine in 2 original articles. The first article (Khuroo MS: Study of an Epidemic of Non-A, Non-B Hepatitis: possibility of another human hepatitis virus distinct from post-transfusion non-A, non-B type. Am J Med. 1980;68:818-24) postulated the existence of another human hepatitis virus of non-A, non-B type which was enterically-transmitted, water-borne and distinct from post transfusion non-A, non-B type (latter identified as hepatitis C virus). The second article (Khuroo MS, Teli MR, Skidmore S, Sofi MA, Khuroo MI: Incidence and Severity of Viral Hepatitis in Pregnancy. American Journal of Medicine 1981:70:252-5) was exclusively dedicated to incidence and severity of disease in pregnant women as depicted from house to house field study. The data showed that this disease has extremely high mortality in third trimester of pregnancy. This article for the first time concfirmed earlier observations of high prevalence and mortality of viral hepatitis in pregnancy so impressively seen in the hospital rounds in India.

The description of this epidemjc led to subsequent transmission (Balayan et al Intervirology 1983; 20:23-31) and clonning (Reyes et al Science 190; 247:1335-9) of Hepatitis E virus. In fact, 13 years later, analysis of the sera collected during this epidemic revealed HEV to be cause of the epidemic (Skidmore et al J Med. Virology 1992;37:58-66). The original paper has been reproduced in the book "Classic Papers in Viral Hepatitis" edited by Christine A. Lee and Howard C. Thomas, Science Press, 1988, page 184-190. On discovery of hepatitis viruses, Robert H. Purcell from NIH Bethesda MD wrote "Simultaneously with these studies, Mohammad Sultan Khuroo, another young gastroenterologist, was studying water borne epidemic of hepatitis in the mountainous Kashmir region of North India. The hepatitis in Kashmir.... Thus the fifth recognized human hepatitis was discovered and initially called epidemic or enteric ally transmitted NANB hepatitis virus and subsequently designated HEV." (Purcell H. The discovery of hepatitis viruses. Gastroentrology 1993; 104:955-63).

Kashmir was hit by a series of large scale epidemic over the next decade and the epidemiology of these epidemics was similar to that reported from the index epidemics. Overall 52,000 icteric cases of viral hepatitis were recorded from these epidemic, with over 2000 deaths. A number of studies were performed during these epidemic to unraval the enigmatic epidemiology of epidemic hepatitis E and these studies have found place in respectable journals. A number of studies were performed on sporadic hepatitis and fulminant hepatitis in Kashmir and major role of HEV in the etiology of these 2 entities was highlighted.

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